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CORRIGENDA

In the article "On the Prognostic Value of the Modified Word Learning Test in Psychiatric Patients over 65", by James Inglis, Ph.D., October 1959, page 1100, the numbers in the four cells of Table I should be:

10	3
0	6

Three lines lower down the new sentence should read:

A value of 9·7 is obtained, etc.

On page 1101 the row headings to Table II should read:

Initial	<i>Functional</i>
Diagnosis	<i>Organic</i>

In the article, "The Treatment of Depressive States with Imipramine Hydrochloride (Tofranil)", by J. T. Leyberg and J. C. Denmark, October 1959, page 1126, the first sentence of paragraph 2 should read:

"The delay in obtaining a therapeutic response and the need for maintaining the patient on the drug for a long time was such that we did not feel justified at present to use Tofranil as a substitute for E.C.T."



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Original Articles

CHANCE AND DESIGN IN PSYCHOTHERAPY*

By

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THE purpose of psychotherapy does not differ essentially from that of the treatment of sickness generally. It is to relieve distress and promote efficiency of mind while improving the patient's adaptation to the group in which he lives, to their mutual benefit. Before psychotherapy can be prescribed or undertaken, a diagnostic review is necessary of the relationship between the patient's psychophysical constitution and the stresses to which he has been and is being exposed. This relationship is a complex one which involves the effects of previous stresses and the way in which they have been surmounted or have left their mark. The introduction of a third complex entity, the method and personality of the therapist, renders the total situation too involved for detailed comprehension and logical analysis, especially if the therapy is to be of the causal-anamnestic or comprehensive kind which is not content simply to deal with symptoms and their immediate causes. In the presence of this degree of complexity—well beyond the range of mental encompassment by one mind at one time—the psychotherapist must walk in humility, for he can rarely feel justified in thinking that he knows exactly what is going on.

Psychotherapy cannot, therefore, be compared to the treatment of a physical disorder where the pathology is well understood and where a single agent can remedy the fault with a minimum of side-effects. This does not reduce its practical usefulness. Even if the statistical examination of large groups has blurred the clarity of its individual successes, there is no doubt that many patients benefit from psychotherapy. It is, on the other hand, a form of treatment which may have side-effects and is not without complications. To be a psychotherapist, optimism is needed as well as skill, and pre-occupation with possible side-effects and complications is not so easy for the optimist. This is not to say that they are to be ignored.

The operation of spontaneous healing, the *vis medicatrix naturae*, is not confined to physical disease. The passage of time and the effect of a benevolent relationship with another human being conduce to improvement more often

* Read at an open meeting of the Psychotherapy and Social Psychiatry Section of the Royal Medico-Psychological Association, Glasgow, July, 1959.

than not in neurosis, so that psychotherapists are not infrequently confronted with a patient who has recovered for reasons unknown to them. The temptation to rationalize in favour of their own chosen method is great.

A psychotherapist, if he assumes that some kinds of psychotherapy at least are worthwhile and at the same time realizes that a detailed knowledge of the whole constitution *vs.* environment situation is out of the question, can approach the problem of complexity in a number of ways.

1. He can limit the field of operations. An example of this would be to confine himself to the removal of a symptom by conditioned reflex methods. Restriction takes place also where one major field of activity is explored in detail on the assumption that a change in attitudes in this field will be carried over into other attitudes to life. The analysis of an inferiority situation or a transference analysis are wider examples of this approach.

2. He can adopt a mathematical attitude to complexity, i.e. he can look for generalizations which are mainly true and base his therapy on these. The human brain is particularly suited to this exercise, although it does not operate at a high level of efficiency. It can arrive at valuable generalizations at the expense of a certain number of errors. When the consideration of a situation rich in detail reaches a certain level of involvement, a form of unconscious statistical thinking comes into play, but the individual is now no longer able to know how he arrives at the result and the operation achieves the status of an act of intuition. A great many creative discoveries can be traced to acts of intuition where the thinker has accepted the duty of checking his hunches against the facts of observation. Psychotherapy benefits from an intuitive approach, provided that, to reduce the possibility of false intuitions and wrong interpretations, the therapist does his best to test his conclusions against the realities of the situation. If this reveals that they fail by the only possible standard, i.e. if they are not likely to help the patient, it is his duty to emulate the scientist, scrap his first conclusions and try again.

3. While the classical mechanisms of psychopathology may be easy enough to understand, the genesis of any given psychoneurosis is determined by a large number of factors peculiar to the individual. One way of overcoming this difficulty is to assume a certain degree of psychopathological uniformity and to develop a single working hypothesis which is likely to apply to as many individuals as possible. It is this approach which has led to the theories of the different schools and their variations. The danger here is that of an exclusivism which ignores the exceptions. The psychotherapist who is rigidly attached to one approach is, however, fortunate in that if a patient is going to recover, such is the catholicity of the human mind that he will often do so as well with one system of psychopathology as another.

4. The fourth method is for the therapist to abandon the attempt to understand what is going on and to believe that an undirected analytical review by the patient of his life and attitudes can do nothing but good. His aim will be to intervene as little as possible. One can only say of this approach that it takes a great deal of time and that in the event the theories of the analyst usually become communicated to the patient at some stage. If, in fact, the therapy were entirely non-directive, the work of the analyst could only be regarded as unskilled.

THE PLANNING OF PSYCHOTHERAPY

It will thus be seen that in planning the psychotherapy of any one patient one may adopt anything from a relatively rigid scheme to an entirely free

relationship and that the therapist can play a strongly positive or an almost negative role. If insight is to be the objective, it is necessary to point out that it must be the patient's insight. It may be that the ideal of insight is overstressed by psychotherapists. Few people have very clear insight into the motives of their daily behaviour and yet they are able to achieve a satisfactory adaptation. If recovery with insight is preferable on theoretical grounds, a recovery without full insight may be equally satisfactory provided that it achieves the practical objectives of psychotherapy. Psychotherapy is for the relief of the patient's sickness, not the satisfaction of the therapist or the vindication of his theory. If ideal results cannot be achieved, the patient can at least be brought within range of full recovery. The general aims of psychological treatment may be summarized as follows:

TABLE I

The Objects of Psychotherapy

- Relief of mental tension and its consequences.
- Removal of functional disabilities.
- More efficient use of mental potentialities.
- Independence, especially to solve own problems.
- Improved adaptation to circumstances.
- Insight, if this helps to prevent relapse.
- Increased capacity for responsibility.
- Induction of a hopeful and positive attitude to problems.
- Creation of a reserve to meet future stresses.

The course of treatment must be constantly under review in the light of its progress towards these objectives. Psychotherapy must also conform to a basic principle of all treatment, that of *primum non nocere*, i.e. that care must be taken to avoid doing harm by the induction of side-effects in the form of irrelevant activities or attitudes which may be a handicap to the patient's general adaptation. To this extent at least, design is necessary, for one does not wish to leave the future of a human mind to chance any more than one would a human life.

CHOICE OF METHOD

A necessary preliminary to psychotherapy is the matching of the type of illness in the kind of person with the available kinds of therapy and of therapists. The main kinds of psychotherapy may be arranged for convenience on an arbitrary scale according to the extent to which they are imposed upon the patient, or the patient himself solves his problem through his own efforts and insight. The scale *Symptomatic-Comprehensive* approximates to this.

TABLE II

Methods of Psychological Treatment

(Arranged as a scale)

Brief and Symptomatic

- Legal or other sanctions.
- Reproof, moral lecture.
- Direct suggestion.
- Suggestion with vehicle.
- Hypnotic suggestion.
- Reassurance.
- Advice and counselling.
- Supportive supervision.
- Re-education.

Imposed therapy

Reconstructive counselling

TABLE II—continued.

Rehabilitation.	Conditioning and rehabilitation
Resocialization.	
Conditioned aversion.	
Other C-R methods.	
Therapeutic scrutiny.	Anamnesis and abreaction
Abreactive techniques.	
Narcosynthesis.	
Free group discussion.	Review and re-synthesis
Play, art and other media.	
Didactic group therapy.	
Persuasion technique.	
Distributive analysis (Meyer).	
Interpretative analysis.	Personal reorientation
Shorter methods of analysis.	
Free-association analysis.	
Logical analysis.	
Comprehensive and Analytic	

Once the general method has been decided upon, it is possible to think of differences of emphasis within the technique used. Some of these are here given in the form of paired descriptive terms which are more or less opposite.

TABLE III
Polarities in Psychotherapy

Imposed	Analytic, anamnestic
Logical, persuasive	Cathartic, intuitive
Direct	Projective
Ego-analysis	Transference analysis
Individual	Group therapy
Specified goals	Generalized
Symptomatic, supportive	Depth and character analysis
Insight therapy	Affect therapy
Interpretative	Free
Integrated with non-semantic methods	Isolated
Social adaptation emphasis	Patient-centred
Advice and direction	Non-directive
Causal	Purposive
At work	In-patient regime

A central decision which has always to be made is whether it will be sufficient to deal mainly with a previously selected (and partially isolated) aspect of the personality in which the maladaptation appears mainly to lie. The difference between the shorter and more restricted methods and those which are more comprehensive where the personality is concerned is not of degree but of kind so that, after diagnostic exploration, a definite choice has usually to be made. If it is not made, the therapist may well be embarking on his task with no clear idea as to method or objective. In making this decision the general characteristics of the "shorter" and "depth" methods of individual psychotherapy have to be considered in relation to the patient's needs. They are given in the form of a table (Table IV, page 5).

While diagnosis in the sense of providing a label for a morbid state has only a restricted application to psychoneurotic breakdown, it is usually possible after the initial examination to produce a provisional formulation which allows of a rough classification of the illness in terms of those conditions known to respond to psychological treatment and those which have been found to make

TABLE IV

Comparison of Symptomatic and Comprehensive Methods of Psychotherapy

Shorter Methods	"Depth" Methods
Limited aim of relieving presenting symptoms and their immediate causes with return to a relatively unmodified way of life.	Aim is to change basic attitudes rather than present symptoms. May lead to major alterations in relations with environment and with other people.
Main concern with the "here and now" problems and the immediate fears, conflicts and frustrations which underlie symptoms.	Causal-anamnestic approach at outset followed by analysis in accordance with one of the orthodox methods.
Insight may be superficial or limited to fields of immediate relevance.	Aims at a high degree of general self-insight as to causes and goals.
Effects on symptoms may be dramatic—on attitudes minimal.	Stable new attitudes evolved, the effect on symptoms being incidental.
Therapist may adopt dominant role, controlling the direction of the therapy, interpreting and using suggestion.	Therapist may accept changing relationship with patient but mobilizes the latter's own resources to solve his problems for himself.
Patient need not be capable of understanding finer points or of considering abstract matters.	Patient must be capable of some abstract thought and have the drive necessary for self-examination.
May be used in the presence of constitutional defect or organic nervous disease.	Not indicated in psychopathy, low intelligence or progressive organic nervous disease.
May be combined with physical treatment, rehabilitation methods and group activities.	Is essentially personal, individual and psychological. Difficult to integrate with other approaches.
Danger of superficial recovery, false insight, pointless abreaction and relapse with new symptoms.	Carries danger of egocentricity, morbid introversion and unresolved transference.
May be combined with appraisal of social circumstances and advice on adjustment of environment, employment, etc.	Changes in his circumstances may be made by the patient as the result of new attitudes.
Economical in time. Less disturbance of usual way of life.	Time-consuming. Life must be to some extent oriented about treatment.

little lasting response. The following list of psychiatric disorders begins with those which are likely to recover even with relatively inept treatment and ends with conditions in which psychotherapy has been said to benefit but in which it has not been found possible to prove that this is so.

TABLE V

Conditions Benefited by Psychotherapy

(In descending order of response to treatment)

Panic, amnesia and other psychological escape mechanisms.
 Functional disabilities—hysteria.
 Recent tension and anxiety.
 Reactive anger, despair and protest.
 Inefficient attitudes to physical illness.
 Organ neuroses.
 Psychosomatic disorders of recent origin.
 Inefficient adaptation to depression and decline.
 Disorders of habit—addictions.

Economic barrier.

Depression and hypochondriasis.
 Obsessions and impulses.
 Ingrained disorders of character.
 Major psychoses, including schizophrenia.

Psychotherapy can be attempted with almost any patient with whom it is possible to communicate, verbally or otherwise. On the other hand, the number of experienced psychotherapists is quite small and in a health service at least it is desirable that they be employed in such a way that as much good shall be done to as many patients as possible. At a certain point in the list above, therefore, a line must be drawn below which therapy is likely to be uneconomic. Of the patients chosen for individual psychotherapy, those at the top of the list might qualify almost automatically and those further down should be considered on their merits with special reference to whether group methods or non-semantic treatment may do as well or nearly as well. Psychotherapy will necessarily be favoured in those conditions in which other methods of treatment are inapplicable. In the following groups wholly physical treatment alone has little more than symptomatic aid to offer.

TABLE VI

Conditions in Which Psychotherapy is More Efficient than Other Methods

Organ neuroses (effort syndrome, mucous colitis, gastric neurosis, etc.)
 Anxiety of very recent origin.
 Recent hysteria with evidence of anxiety.
 Isolated obsessions in children.
 Conditioned neuroses (fainting on injections, etc.).
 Minor addiction in sound personalities.

There are certain other psychoneuroses in which, although psychotherapy is often attempted and in which it may comfort and support and although material of psychopathological interest is often elicited in profusion, the practical results of intensive and detailed psychotherapy are disappointing. It has taken a great deal of wasted time to come to the conclusion that comprehensive therapy in the following is likely to be uneconomic:

TABLE VII

Conditions Giving Disappointing Results with Comprehensive Psychotherapy

Multiple obsessions and compulsions.
 Chronic phobic anxiety.
 Adult homosexuality.
 Chronic and degenerative hysteria.
 Severe stammering.
 Endogenous depression.

That these conditions are not altogether relieved and often not even improved by psychoanalysis and comparable methods has gradually become clear and it is the inclusion of patients with these disorders which has probably influenced the statistical studies of the results of long-term psychotherapy so that its major successes are lost to sight. That these conditions do not respond to the point of complete relief does not mean that they are not helped, but it is probable that symptomatic methods may actually help them more with less expenditure of time. By contrast, constitutional loading, psychopathic personality or chronic organic nervous disease, although they are contra-indications to comprehensive methods, may even make a response to shorter methods more likely. The objection usually raised, i.e. that the symptoms may return, is only valid if they return at once. Follow-up studies in chronic hysteria, for instance, suggest that two or three episodes of brief psychotherapy in a 20-year period are a small price to pay for a reasonably independent adjustment to life in a constitutionally vulnerable individual.

Apart from giving weight to general evidence of psychopathic personality or severe constitutional vulnerability, it is important when deciding on the appropriate treatment for a psychoneurosis, to determine whether the symptoms are due to an isolated maladjustment or whether they are based on a more generalized state of psychoneurotic maladaptation. In making this decision the following general features found in those predisposed to or habituated to psychoneurotic breakdown form a sort of recognizable neurotic constitution.

TABLE VIII

General Features of the Neurotic Response

Failure to remain efficient under stress.
 Presence of persistent tension or anxiety or of their somatic effects—or of detachment.
 Exaggeration and facilitation of psychological defence-mechanisms.
 Loss of ability to give priority to problems according to extent to which they threaten integrity of the psyche.
 Failure to pay attention to unwelcome information from without and within.
 Inability to decide firmly on conflicting issues. Uncertain or unrealistic goals.
 Disproportionate emotional responses. Facility in rationalization.
 Inability to cast off past attitudes and accept maturation or changed conditions.
 Return to childish attitudes.
 Unhappiness, sense of fatigue. Discontent easily aroused.
 Lowered adaptive efficiency due to anxiety, fear for the future, dissociative states, functional disabilities, despair, self-preoccupation, dependence and invalidism.
 Egocentricity at the expense of responsibility.

Once a therapeutic situation has been established, improvement may come about for a variety of reasons. Except in a very strictly planned attack on limited symptoms, the therapist cannot hope to be in control of every possible favourable influence. He can, however, be ready to press an advantage which chance and his relationship with the patient make for him. All therapy must thus be to some extent opportunist. A number of factors which may bring about unplanned improvement may be mentioned at this point.

TABLE IX

Factors Which May Bring About Unplanned Improvement

Incidental reassurance that the illness is not unique and that the therapist thinks it worth treating.
 Effects of formulating the problem in order to communicate it.
 Acceptance of explanations which are inaccurate but which serve as working hypotheses.
 Provision of immediate goals which divert the patient from his stress-producing situation.
 Endogenous mood-change.
 Solution of minor conflicts which unconsciously change attitude to major ones.
 Effects of the discipline of the regular session and any regime prescribed with it.
 Recall of false memories with beneficial catharsis.
 Training in an attitude of anamnestic self-enquiry which allows the patient to solve his own problem.

If all incidental effects were beneficial, the only purpose of planning would be to reduce the time taken, i.e. to make psychotherapy more efficient and economical. Unfortunately there are complications which may leave the patient worse off from the point of view of personal and social adaptation than when he started.

TABLE X

Complications to be Avoided in Psychotherapy

Unresolved transference.
 Habitual catharsis.
 False insight and paranoid reaction.
 Excessive dependence. Psychological invalidism.
 Use of therapy as escape, or as excuse.
 Precipitation of psychosis.

In the course of treatment it is inevitable that a variety of changes in attitude and in the mental mechanisms used will make their appearance. These will arise partly in the maladjustment itself and partly from the patient's response to the therapeutic situation. It is advisable, if he is to understand these changes, for the therapist to observe and record at successive stages, events such as the following so that he can adjust his own role accordingly in the light of his objectives:

TABLE XI

Changes in Attitude in the Course of Psychotherapy

Positive and negative transference.
 Suggestibility and negativism.
 Independence—demands for advice.
 Periods of rationalization and demands for explanation.
 Selective inattention and evasion of central issues.
 Phases of apathy. Cathartic phases.
 Conversion of anxiety—crises of anxiety.
 Variations in the presenting symptoms.
 Use of therapy as an escape from conflict.

It is necessary to bear in mind any possible side-effects of psychotherapy which may reduce the usefulness of treatment when its results are considered simply in terms of adaptation. They will influence the decision as to when the patient has got all he can usefully get out of the treatment. The fact that the patient comes to like the therapeutic session or that it becomes a part of his established routine, or that further treatment may lead to a psychopathologically more satisfactory insight are not sound reasons for continuing treatment. In fact, it is often difficult to know when to stop or to reduce the frequency of the treatment sessions. "Side-effects" to be taken into consideration include:

TABLE XII

Side-Effects of Psychotherapy

Loss of working time—postponement of decisions about employment, moves, etc.
 Excessive dependence on the therapist or on the system of explanation he uses.
 Habitual egocentric self-analysis.
 Addiction to psychotherapy and lack of an alternative audience.
 Financial effects of treatment.
 An excessively high ideal of what personal adjustment should be.
 Diversion of energy from duty into analysis.
 Permanent acceptance of tendentious explanations.
 Becoming a "psychotherapy bore" who interprets other people's actions.
 Conversion to a school of thought as a substitute for religion, with proselytizing tendencies and determination to become a lay therapist.

THE PLANNING OF RESTRICTED TECHNIQUES

Certain psychotherapeutic operations are particularly suitable for planning in advance. Even if the disability to be treated is related to a defect of the

total personality, the dissociated treatment of single symptom-groups may still be well worthwhile. Treatment by direct suggestion under hypnosis, for instance, may allow a patient to return to work which itself has a beneficial effect on his general adaptation. In general medicine or surgery, treatment is often given which will not cure the patient but which will allow him to make the best use of reduced resources. This is comparable to symptomatic and supportive psychotherapy given to those known to be constitutionally handicapped. Some examples of simple and restricted psychotherapy which can be planned in advance will now be given. They are from my own cases.

1. *Simple Conditioned Neuroses*

These have included such conditions as fainting at the sight of blood, "drying up" in public speakers and vomiting in public vehicles. The example to be given, one of fainting when given injections, illustrates the method used. The process of conditioned extinction was in this case much more thorough than usual owing to the failure of previous treatment. In a suitable subject, a quicker method might have been to give injections under hypnosis, the conditioned extinction method being reinforced by direct and post-hypnotic suggestion. It is worthy of note that tics and compulsive utterances which appear only in special situations appear to recover on this regime in spite of the presence of an underlying cause in central nervous disease which may reveal itself later in other ways.

TABLE XIII

Simple Conditioned Neurosis

Example: Fainting when given injections

I. *Non-Semantic Therapy. (Unabbreviated.):*

Session I:	
Patient lying down	After 40 minutes swab skin
50 mg. chlorpromazine	50 minutes inject 1 c.c. saline
4 gr. sodium amytal	70 minutes inject 1 c.c. saline
	90 minutes inject 1 c.c. saline
Session II:	
25 mg. chlorpromazine	40 minutes inject 1 c.c. saline
3 gr. sodium amytal	80 minutes smell ether and meth.—inject 1 c.c.
	120 minutes smell ether and meth.—inject 1 c.c.
	150 minutes smell ether and meth.—inject 1 c.c.
Session III:	
10 mg. chlorpromazine	10 minutes smell ether and meth.
1 gr. sodium amytal	20 minutes inject 1 c.c. saline
	60 minutes inject 1 c.c. saline
	120 minutes inject 1 c.c. saline
Session IV:	
Placebo I	20 minutes inject 1 c.c. saline
Placebo II	60 minutes inject 1 c.c. saline
	120 minutes inject 1 c.c. saline
Session V:	
Lies down	20 minutes inject 1 c.c. saline
No drugs	120 minutes inject 1 c.c. saline
	180 minutes smell ether and meth.
Session VI:	
Lies down	At once inject 1 c.c. meth.
Stands up	After 10 minutes inject 1 c.c. meth.
Comes up to trolley	10 minutes smell ether and meth.
Imagines TAB injection	10 minutes inject 1 c.c. saline slowly
	10 minutes inject 4 c.c. saline slowly

TABLE XIII—continued.

Session VII:

Injection TAB 0.5 c.c.

Two weeks later:

Injection TAB 1 c.c.

Tetanus toxoid

Time taken, three weeks.

The patient was a man of 26 in good health who had fainted when given injections since the age of 13, when a course given for hay fever had to be abandoned. The patient's sister also had a great fear of injections and was terrified when given them for hay fever. The patient had witnessed this and had then felt faint. He himself feared that he was unconsciously avoiding foreign travel by this means, a view which had been accepted by a psychotherapist to whom he was referred. He was in fact very hesitant to leave his home. After some months of treatment an attempt at inoculation was made. He once more fainted and, shortly after, treatment was abandoned. He clearly had little faith in psychotherapy and for this reason conditioned extinction was carried out very gradually. On completion there appeared to be no residual anxiety or other reason for further treatment. After three years he is well, yellow fever inoculation and vaccination had been carried out and he has travelled a great deal, mainly by air.

In this case the detail is given in full. It is, however, possible in the interests of generalization to represent the aetiology of a simple neurosis and the principle used in its treatment in diagrammatic form. A case of diarrhoea occurring in church in a child will serve as an example.

TABLE XIV

Simple Conditioned Neurosis

II. CHURCH DIARRHOEA:

Aetiology:

1. Anxiety expressed in vulnerable organ.

Bowel $\longrightarrow$ Diarrhoea.

2. Anxiety + Church
- $\longrightarrow$
- Diarrhoea
-
- (unconditioned) (conditioned)

Leads to:

Church $\longrightarrow$ Diarrhoea*Treatment (by extinction):*

1. Different Church
- $\longrightarrow$
- No bowel response
-
- (with sedative)

Repeat with diminishing sedative

2. Leads to:

Church $\longrightarrow$ No bowel response
(deconditioned stimulus)2. *Organ Neuroses*

An outstanding example of the planned treatment of an organ neurosis is the large-scale management of Effort Syndrome which took place after a reappraisal of the aetiology of this condition in military conditions in 1940. Neglecting its individual variations, the psychogenesis as it occurred in new conscripts can be represented by the following schema.

TABLE XV
Aetiology of an Organ Neurosis

EFFORT SYNDROME IN RECENT CONSCRIPTS:

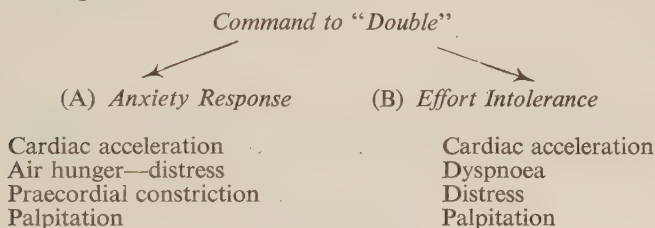
Background Conditions:

- Protected previous environment.
- Poor effort tolerance and fitness.
- Anxiety mainly felt in c.v. system.
(Heart is constitutionally vulnerable organ.)
- Previous attention drawn to heart
(e.g. murmur, or rheumatic pains in childhood).

Recent Predisposing Causes:

- Anxiety and loss of sleep in barracks.
- Call for unaccustomed effort.
- Fear of humiliation, punishment, overstrain.

Conditioning Process:



Established Condition:

- Effort produces combined syndrome (A+B)
- Patient then worries about his heart
- Symptoms perpetuated by secondary gain.

On this basis the syndrome, which was remarkably uniform in a very large number of troops, could be dealt with by means of a regime which combined conditioned inhibition with rehabilitation. Essentially the process was as follows:

TABLE XVI
Treatment of an Organ Neurosis

EFFORT SYNDROME:

1. Counteract Secondary Effects:

- (a) Reassurance, without reservations.
Single, final cardiac examination.
- (b) Discourage secondary gain
Explain condition is always treatable.
Assure that discharge from service is not considered in any circumstances.

2. Transfer to Special Unit:

Eliminate conditional stimuli:

- At first: no sudden commands.
- Reasonable comfort. No injustice.
- Regular life but no sudden efforts.

TABLE XVI—*continued*.*Extinguish conditioned response:*

(a) Non-reinforcement:

Minor but increasing effort in recreational conditions. Increase of effort without commands. Re-training and testing effort response.

(b) Conditioned Inhibition:

Introduce commands when effort response is normal. Test with violent commands.

3. Re-train.

Once improvement had been produced, as it was in the majority, it was possible to decide, on individual constitutional differences, which soldiers were capable of giving full service and which could be exposed only to limited strain. Although in civilian practice cardiac neurosis is often associated with cardiac disease, especially after small coronary thromboses, treatment on the same lines is often remarkably successful provided that the cardiologist is willing to recommend graduated exercise without making over-cautious reservations. The principle that the remaining cardiac muscle must be kept in optimal condition is put to the patient.

Another organ neurosis, mucous colitis, has, in my own experience, rather surprisingly shown a considerable uniformity, the scheme below being a composite from seven cases in the course of six years.

TABLE XVII

Organ Neurosis

II. Mucous Colitis in a spinster of about 40.

Aetiology:

1. Since childhood, bowel active when anxious. (Bowel is vulnerable organ.) History of gain (absence from school, evasion of homework) from diarrhoea.
2. History reveals time-relations of onset and of exacerbations. Current stresses include affair with married man.
 1. This delays possibility of marriage.
 2. It is likely that he will tire of it, but he is too considerate to say so. Life as spinster would be less exacting than present situation.

A state of conflict has been set up:

3. Meeting with man causes anxiety—and diarrhoea. This prevents intercourse. (She feels it may disgust him, so that he will leave her and solve the problem.)
4. General anxiety and colitis increase as no decision is made.

Treatment:

1. Bring conflict to light—anxiety increases.
2. Patient shows catharsis and is convinced of relevance of conflict.
3. Further discussion shows origin of symptom.
4. Patient decides to leave man.
5. Period of vacillation with generalized anxiety.
6. She discusses it with man—he is only continuing out of sympathy.
7. Alternative interests discussed—recovery.

A number of other psychoneurotic disabilities are sufficiently uniform in general aetiology and manifestation to allow of an approach on lines which are mainly predictable. By way of example, a more generalized scheme will be given which is based on the treatment of a number of recent anxiety states in patients under 30.

TABLE XVIII

*Simple Anxiety State of Recent Origin**Aetiology:**Predisposing Causes:*

- Constitutional predisposition to anxiety (with physical over-reaction to stress).
- Previous pathological anxiety.
- Standing conflicts, frustrations, fears.
- Difficulty in making decisions.

Precipitating Causes:

1. Conflict: with no obvious solution.
with no satisfactory solution.
2. Rising tension aimed at bringing about a rapid decision and failing to do so.

Result:

- A pathological tension-response to unsolved conflict.
- Selective inattention to and retreat from conflict (with or without conversion) so that causes are not fully recognized.

Treatment:

- (a) Withdrawal from immediate environment to allow full concentration on treatment. Give task which allows of consideration between sessions.
- (b) Anamnestic approach—circumventing evasions and defence mechanisms:
 1. Conflict becomes evident.
Anxiety increased—with some catharsis.
- (c) Help patient to mobilize issues involved until grounds for decision are plain. Encourage decision, but do not advise.
- (d) Discuss implications of decision (i.e. reality test). False decisions necessitate re-examination. When symptoms improve, encourage to think ahead and emerge with clear goals.
- (e) Return to former environment. Retrospective discussion to ensure insight. Supervise until patient able to deal with problems as they occur.

The examples given will serve to illustrate the view that therapy restricted to the areas or complexes which have been the immediate cause of a psychoneurosis can be planned within the limits of individual variation, provided that therapy is preceded by a clear diagnostic formulation and general plan of treatment. There are, of course, many psychoneuroses which require a prolonged diagnostic investigation in which opportunities for helping the patient will arise and must be taken. In recent psychoneuroses time is usually on the side of patient and therapist alike and considerable economy in effort can be made and some danger of doing harm can be avoided by working to a general plan. In recent anxiety, treatment is urgent if the development of the less reversible features of chronic anxiety is to be avoided. Keeping the patient to the point lowers the incidence of conversion episodes. Such treatment requires considerable alertness and clarity of aim in the therapist. He must above all develop a knowledge of when to leave well alone.

When suggestion is the main instrument in treatment and the part played by the patient is passive and guided, it follows that the technique to be used can be worked out in detail beforehand. Since the effect of suggestion depends not only on the ideas conveyed to the patient but also in the patient's own conception of their meaning, misunderstanding is avoided if the suggestions are made unambiguously and in a definite order. If hypnosis is used it is often wise to write out the plan to be used in advance lest incidental phenomena of the trance-state such as spontaneous catharsis, amnesia or hyperventilation

interfere with the intended course of treatment. When several suggestions are made at different sessions it is essential to keep a written record lest they prove contradictory in the mind of the patient. The process by which the success of one suggestion enhances the effectiveness of the next depends to a great extent on the avoidance of unintended effects.

THE SIGNIFICANCE OF MOOD

Of all the factors which introduce an element of chance into psychological treatment, changes in mood are probably the most important. The majority of patients suffering from psychoneurotic breakdown are subject to changes of mood of a significant degree while endogenous depression is perhaps the commonest of all psychiatric disabilities. Further, endogenous mood-change may make the difference to whether a given psychophysical constitution can adapt itself successfully to the stress it encounters. A considerable number of patients presenting themselves with symptoms of recent anxiety or hysteria have been dealing successfully with fears, conflicts and frustrations until a mood-change in the direction of depression renders their burden insupportable. While mood change is very often reactive, it may also vary with the metabolic state. Depression may be induced by infective states or by the drugs used to treat them or they may spring from endogenous causes at present little understood. Contact with patients in the professions whose lives are made difficult by manic-depressive variations of moderate degree indicates that in some the first depression has often precipitated an illness with psychoneurotic features which has been subjected to psychoanalytic treatment. In some of these no progress has been made for several months after which there has been a sudden improvement. As one Civil Engineer said, "I suppose it was the cumulative effect of the analysis which I admit I thought was getting me nowhere—I suddenly found the ability to examine and solve my own problems and I just got better." His subsequent history makes it extremely probable that his depression just came to an end and the analysis got the credit. Another patient, a lawyer in whom nearly four years of analysis was terminated by a classical attack of hypomania, said "The attempt at analysis in my depressed periods was a long-continued torture in which I dragged the depths of my mind for more and more sources of guilt-feelings—we made no progress as salt was steadily rubbed into my wounds." The sadness of these therapeutic efforts, in this case, lay not only in their lack of success, but in their economic consequences for the patient and their sheer irrelevance. The recognition of mood-change in the course of comprehensive therapy does not always call for abandonment of the treatment, but it does call for adaptation to the patient's variations in drive and outlook on his problems. In the course of detailed psychotherapy, changes in the direction of mild elation with relief of tension occur too frequently to be due to endogenous causes alone, but whatever their cause they can often be exploited in the patient's interests because of the fresh insights which come with them.

WHEN TO STOP

Much of the interest of psychotherapy to the therapist lies in the prospect that in the end the mystery of the illness will be explained and the loose ends will be tidied up as in a good detective story. But just as the surgeon cuts and stitches in the expectation that nature will heal and strengthen, the psychotherapist, if healing and not research is his object, need do no more than bring his patient to the point where he can heal himself.

It is not always easy, when the planned objectives have been attained, to know when to replace participation by observation. Even more is it difficult to make the decision when it has become clear that the objectives are not going to be attained and that therapeutic time might be better employed elsewhere. Some of the reasons why comprehensive psychotherapy is carried on when no major improvement can be expected may be summarized:

TABLE XIX

Factors which Lead to a Continuance of Psychotherapy in Spite of Its Failure to Achieve Its Objects

Initial improvement raising hopes.
Emergence of psychopathologically interesting but therapeutically useless material.
Unresolved transference.
Confusion of causal with supportive treatment.
Bilateral reluctance to admit failure.
Mercenary considerations.
Therapeutic session has become patient's main interest.
Therapist's belief in universal application of his method.
Absence of alternative treatment.

THE ADJUNCTS OF PSYCHOTHERAPY

There are psychotherapeutic purists who feel that when a patient is referred for treatment by their particular method, to assist the cure by other means such as physical treatment, is rather comparable to shooting a sitting bird out of season. But psychotherapy is not a sport, it is a part of the vital battle of adaptation in which no holds are barred. Any kind of ammunition, pharmacological, emotional or semantic, is permissible if it can be used to support the patient's constitution against the rebel forces of unreason. It is better, too, if the different methods can be used so that they do not get in each other's way. A unified command leaves less to chance.

The principle of separating the individual approach to the patient's psyche from the treatment of the whole man has many adherents, but it can at least be questioned in many instances, and in planning treatment it is well to consider the adjuncts which may contribute to the success of psychotherapy. They are here summarized in tabular form.

TABLE XX

The Adjuncts of Psychotherapy

Regime. Occupation. Diversion.
Environmental Adjustment.
Health. Medical. General fitness.
Rehabilitation—Retraining—Education.
Homework—Writing appraisals—Prescribed reading.
Resocialization—Groups—Clubs.
Pharmacological—Abreactive.
Mood-changing.
Sedative and symptomatic.
Isolation. Weir-Mitchell. Sensory deprivation.
Non-Semantic. Conditioned inhibition.
Aversion. Play.
Religious. Reading. Retreat. Discussion.
Physical. Faradism. E.C.T.
Supervision. Probation. Antabuse.

In psychotherapy, as in love or in war, there must always be an element of chance. When art and science combine in the treatment of an individual, it is the

function of science to reduce that element to a minimum. The therapist is no mere spectator even if his is not the major role. In that he participates and often holds the initiative, psychotherapy is a stress to the psychotherapist whose task is to hold his patient's interests in view and manifest his role of protector, receiver and friend by helping him over each obstacle in turn. Like a father who teaches his child to walk, he is content to know that when he himself has been forgotten the child will walk unaided.

BODY IMAGE AND SELF-CONCEPT IN SCHIZOPHRENIA

AN EXPERIMENTAL STUDY

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DISTURBANCES of ego, self-concept and body-image have always been regarded as central in the psychopathology of schizophrenia. The passivity phenomena, *automatisme superieur* of the French authors, are indeed very common in this disease. There is a disturbance of the self which is shown in depersonalization and in feelings of influence and passivity. The boundaries of the self become loose or blurred and the patient may feel, for example, that parts of his body do not belong to him or that he is part of the plants, animals, clouds, other people or of the whole world and that they are part of him. He may feel at one with the whole of mankind. Self-concept is closely related to what has been termed "body image" or "perceived body". Head (29, 30) has shown that what he called "body schema" is very important for motor co-ordination and performance of purposeful movements and also for orientation in space. Schilder (53) in his monograph has analysed the problem of body-image in great detail. He has found in the idea of the body image the basis for the body or physical ego. He follows Head in stating that the body image consists of the proprioceptions of the whole body and that it changes with the body's varying postures. Yet neither Head's body schema nor Schilder's body image are identical with the body ego. The body schema represents the constant mental knowledge of one's body; the body image is the changing presentation of the body in one's mind. Throughout the changes of the body image there is an awareness of continuity of one's body, a sense of basic identity and oneness. This constitutes the bodily or physical ego. The body ego in its turn is the basis of a wider "self" which can be called self-concept or selfhood. This self-concept or selfhood contains, in addition to the awareness of the continuity and the identity of one's own body in spite of its constant change, the awareness of the continuity of one's self as a person in spite of constantly changing relationship with the external world, and in spite of the playing and taking different "roles" in social interactions. According to Mead (38) and Coutu (16), selfhood is a social phenomenon and emerges only through interaction with other people, through "taking their roles" and viewing oneself from their point of view.

Self-concept is linked up with the problem of one's identity and continuity and also with the problem of one's individuality, by which is meant perception of oneself as an independent entity in the environment. It embraces, therefore, the concept of ego as the witness, the experiencer or the subject, with which philosophers since Descartes were concerned and which in psychological theory was stressed by Brentano's school of "act psychology"; it also embraces the

concept of ego as the nodal point in the integrative process of behaviour with which personality theorists, psychoanalysts, and gestalt psychologists were mainly concerned. The first aspect of the ego is equivalent with the philosopher's subject, the second with the philosopher's object. The ego as the subject may be equated with the English pronoun "I" and the ego as the object with the English pronoun "me". To put it in other words, "ego" in its objective aspect is concerned with relatedness to the environment with establishing a point of reference in physical or social space or in flow of time. In terms of field theory it is a point determined by the totality of the field forces. This point of view is most typically represented by Koffka (34) who describes "ego" as a certain point in the psycho-physical field, from which phenomena are referred as being in front, behind, above and below, and so on. On the other hand, "ego" in its subjective or "I" aspect is concerned with the ability to detach oneself from the environment, to break down the environment-bondedness, to attain an autonomy from the environment, to be an independent entity and to act as a free agent.

An analogy may be drawn from physics. The experience of self is like a physical event which can be described either from the point of view of wave mechanics or the point of view of quantum mechanics. In the first case an event is just a focal point in a physical field; in the second case it is an independent and enduring entity. In social psychology the distinction between "I" and "me" was particularly stressed by Mead (38). He identified "I" with subject and "me" with percept of oneself as seen by others in social group. To quote this author's own words: "The 'I' is the response of the organism to the attitudes of the others; the 'me' is the organized set of attitudes of others which one himself assumes. The attitudes of the others constitute the organized 'me' and then one reacts toward that as an 'I'".

Both these aspects of self experience are important in ego psychology and its proper integration and functioning depend on the proper balance of these two aspects. The development of selfhood and ego has been studied by many child psychologists; for example, Piaget (44), Preyer (46), Moore (40), Cooley (13), Gesell (26), Shinn (55), Fisher (20) and Bain (5). All these studies point to the gradualness of ego development, to the importance of body image, to the importance of perceptual and conceptual constancies and of interaction with other people. Piaget (43) describes the phase of egocentrism in the development of selfhood. Cameron (11, 12) follows Mead in stressing the importance of role-taking in the development of self in relation to the outside world. The common factor in both egocentrism and deficiency of role-taking is the inability to look at oneself from an outside point of view, an inability to distinguish between "I" and "me".

Many of the above-mentioned authors studied the language of children, particularly the usage of pronouns as a means to attain insight into the development of selfhood in children. Thus Bain (5) has found that in the earliest stage of speech development the child does not use pronouns referring to self, describing himself in the third person. In a later stage he develops the concept of "me" and "mine" and in a still later stage he develops the concept of "I".

There is ample clinical evidence that self-concept is disturbed in schizophrenia. Abnormalities of body image, delusions of changing sex, delusions of body disintegration, and depersonalization are very frequent in this disease. However, even more important and pathognomonic for schizophrenia are disorders of selfhood, both in its subjective and objective aspects. Some authors have stressed disorders of the experiencing ego while others have stressed

disorders of the experienced self. Still others have emphasized the breaking-down of the boundaries between self and non-self in schizophrenia. Bender and Keeler (7) in an experimental study have found that schizophrenic children have particular difficulty in determining the periphery of their bodies. Fisher and Cleveland (21) have recently developed a method of scoring the Rorschach test by which they determined the definiteness of the body boundary. They have found that schizophrenic patients give very few "body boundary" responses on the Rorschach test in comparison with normal controls and other psychiatric patients.

The disorder of objective ego or "me" may manifest itself in the lack of a sense of continuity, in the loss of boundaries of self*, in misperception of one's identity and in abnormalities of role-playing and role-taking. Weinberg (62), a sociologist, believes that inefficient role-taking protects the schizophrenic from looking at himself, and thus permits him to retain his autistic ideas and delusions. On the other hand a disorder of subjective ego manifests itself in feelings of passivity, in impersonality ("itness" quality) of one's inner experience. Both Schilder and Federn (53, 19) use the concept of cathexis and libido to explain the integration of experience into the ego system. Federn postulates that schizophrenia begins with an impairment of ego cathexis; the ego boundary in particular can no longer be held cathected to its normal extent, leading to a weakness of ego system and its eventual disintegration. Schilder (54) cites Minkowski who believes that "the immediate experience of experiencing oneself" is impaired ("*Le schizophrène, par contre, sait où il est, mais le moi-ici n'a plus sa tonalité habituelle*"). Sherif and Cantril (52) developed a theory of ego psychology in which they substituted the term ego-involvement for that of ego-cathexis. This gives an adequate description of the phenomena concerned, avoiding at the same time any assumption as to the existence of "mental energy" or "libido". These authors explain ego as a system of organized attitudes and values, which is responsible for the style and consistency of one's behaviour. They describe schizophrenic illness as characterized by the radical breakdown of the more usual frame of reference which had been developed to give meaning to the environment. These frames become inadequate and inconsistent. When these standards for judgment and action collapse, the ego collapses, because these frames with all the emotional overtones of value judgments they contained were so integral a part of the self.

Disorders of self in its objective aspects are common in clinical literature. Here we include beliefs as to the changed appearance of bodily organs or to their being empty, hollow, or weightless. Angyal (3, 4) makes the interesting suggestion that some of these seemingly bizarre ideas about one's body may have a sensory basis. He uses the example of certain tactile illusions whose localization depends upon the clarity of one's picture of the bodily self. Thus one would expect that the schizophrenic whose schema of his bodily self is impaired would be more susceptible to such illusions as have been described by Pongo and Kohnstamm. In the Kohnstamm illusion, for example, one's arm appears weightless and seems to rise of its own accord.

Some of these changes in perception of one's own body may be attributed to a breakdown of perceptual constancy in schizophrenia. Experimental

* The boundary of self in the "me" or object aspect of self is not really clear-cut. There is a gradient of diminishing ego involvement or ego cathexis from the "centre" to the "periphery" and the transition from self into non-self is gradual. Nevertheless, the outer boundary of the self may be described as a line where the ego involvement becomes very low. Self in its subjective, "I", aspect has really no boundary, because it cannot be represented by a special model; there is rather an autonomy of "I" and of "not I".

evidence (15, 58, 59, 60) has shown that various constancies are impaired, and it would account for believing that one's arms or legs were shrunken, and that limbs or fingers frequently expanded or contracted in size or changed in coloration. Such perceptual phenomena can doubtless produce feelings of estrangement from one's own body. The schizophrenic who claims that the faces of people around him change in colour or size, or that the world moves when he turns his head, may be expressing a view of the world perceived literally, i.e. without the operation of the various constancies of size, colour, shape, etc. As far as we know, no one has investigated the ego and self disturbances in schizophrenia from the standpoint of impaired perceptual functioning. It seems apparent that if the schizophrenic is unable to maintain concepts as well as normals, we should expect him to experience difficulty in recognizing other people and maintaining his self-concept in an ever-changing world.

There is also the view that the schizophrenic experiences a breakdown of the boundaries between self and non-self. Sullivan (56) wrote that the schizophrenic suffers from the fear of becoming "a form of nothingness" by collapse of the self. Balint (6) states that the problem of reality testing in schizophrenia is essentially one of deciding whether a sensation comes from within or without. Such difficulties can underlie delusions of reference, feeling of influence and magical thinking.

Be as it may, the problems of ego boundary, ego identity, ego belongingness, body image and subject-object relationship are crucial for psychopathology of schizophrenia. Similar disturbances occur in mescaline and LSD-induced psychoses: body image is awry, ego-boundary undergoes change and may disappear altogether, subject-object relationship becomes disturbed. Savage (51) made a systematic study of the effects of lysergic acid (LSD) on the perceived body. His subjects reported that their bodies lost symmetry and became plastic with fluid boundaries.

This paper reports several studies which attempt to test experimentally the validity and generality of some of these clinical reports of disturbances of self-concept and body image in schizophrenia.

There are few established methods of studying self-concept systematically. However, many of these clinical accounts do provide some direction as to which avenues may prove the most fruitful. For example, one of the observations made repeatedly in the literature is that schizophrenics react to mirrors in unusual ways. Abely (1, 2) was apparently the first to call attention to this and published several accounts of "le signe du miroir". Delmas (17), Ostancow (41), Galant (24), and Knoos (35) also noted this behaviour in schizophrenic patients, but Rosenzweig and Shakow (48) were the first to study the frequency of the symptom in a sizeable group of patients. However, even these authors did not use the mirrors in any systematic way or obtain verbal reports of the patients' reactions to their reflections. Thus the use of mirrors is a very promising method for exploring self-concept and at the same time a relatively unexplored one when used in a systematic fashion.

METHOD

To explore several facets of the person's self-concept, we employed a number of procedures, some of which are already found in the literature while others are of our own making. The first of these involved the person's reactions to his reflection in a large three-panelled mirror. The dimensions of the two

outside panels were 5 feet 9 inches $\times$ 16 inches, while the centre panel was 5 feet 9 inches $\times$ 18 inches. The two side panels were at a 120° angle from the centre panel. All subjects stood 12 inches from the centre panel and were asked the following questions:

1. What do you see?
2. What else do you see?
3. How many people do you see?
4. Do all these people look alike?
5. Which is the real you? (Point to it.)

All answers were recorded verbatim. The subjects in the first study were 34 schizophrenic and 18 non-schizophrenic patients in a 1,500-bed mental hospital, and 29 normal subjects, all of whom were employees of the hospital, i.e., painters, secretaries, nurses, accountants, etc. No psychiatrists, psychologists, or physicians were used in the study. The average age of the schizophrenic patients was 38.6 years (range 21–55), of the non-schizophrenic patients 42.3 (range 17–58), and of the normals 37.5 years (range 17–66). All of the schizophrenic subjects had participated in other research studies and were known to be reasonably co-operative and average or above in intelligence.

After these five questions were asked, and the answers were recorded, the subjects were asked to describe the person in the mirror as if they were looking at a photograph of someone else. These descriptions were scored independently and are called "Part B" of the first study, while the answers to the five questions are called "Part A".

As this study had been strictly empirical in that no prior hypotheses had been formulated, it was decided to conduct a second study along similar lines, but with a slightly modified procedure. This is referred to as "Study Two".

In the third study, the subjects were tested with the W-A-Y technique. This involves asking the person to give three answers to the question, "Who are you?" and is considered by Bugental (10) and others to be a promising way to explore the person's concept of his social roles. It was felt that this technique would complement the mirror descriptions which dealt with primarily psychological dimensions.

The fourth study again returned to the three-panelled mirror but used a slightly different procedure. This time the upper part of the centre panel was covered with white paper so that the subject could see the lower part of his body but could not see his head. The instructions were as follows: "You see your reflection in the mirror; the head is missing. Draw the missing head in its real size." When the patient finished the task, the drawing paper was removed and replaced by a larger sheet which allowed the subject to perceive only the lower part of his body up to the waist. He was instructed to draw in the missing parts including his head and left hand, which was placed on his chest. The following body measurements were taken: height and width of head, width of shoulders, length of forearm, and length and width of hand. Next the subject was given the Draw-a-Person test. Finally his left and right orientation was tested. The experimenter pointed to the subject's left arm and asked him whether it was left or right. Then the experimenter faced subject, lifted his own right arm and asked whether it was the experimenter's right or left arm. Next he pointed to one arm of an assistant whose back was turned to the subject and asked whether it was the assistant's left or right arm. Next the subject had to identify his right and left side in three different reflections of himself in the three-panelled mirror.

RESULTS

Study 1

The number of reflections reported by each of the groups is shown in Table I. It can be seen that both of the patient groups reported significantly fewer reflections than the normal group. However, all of the distributions were bimodal.

There was no difference in the location of the real self. It was located either in the central reflection in front of the subject or in the subject himself. The first was more common. The schizophrenics gave poorer and less complete descriptions of their reflections than the other groups. Some of these descriptions given by the schizophrenic patients were quite bizarre.

TABLE I
Number of Images Seen

				Schizophrenics	Normals	Non-schizophrenic Patients
Below 11 images	..	..	..	25	5	12
Above 11 images	..	..	..	9	24	6
Chi-square	..	..	..	$\chi^2=21.88$ (d.f.=2) p 0.01		

The self-description of the groups showed significant differences in the use of first person pronouns. The schizophrenic patients were less likely to use the words "my", "myself" or "me" in describing their images. Although the schizophrenics produced somewhat fewer words than either of the other groups, there was not a significant difference between the three groups in average verbal productivity. These differences were tested by median tests, the results of which are summarized in Table II. "Part A" refers to the answers to the five questions mentioned previously and "Part B" refers to the subject's description of himself as if looking at a photograph.

TABLE II
Number of Words and Self-references

			Part A		Part B*	
		Total Number of Words	No. of Pronouns (Self-references)	Total Number of Words	No. of Pronouns (Self-references)	
Schizophrenics	..	815	78	667	32	
Normals	..	998	123	697	59	
Non-schizophrenics	..	314	52	539	48	
Median count per subject	..	25.5	3.0	28.0	2.5	
Schizophrenics	Above	15	22.5	9	5	
	Below	20	12.5	17	21	
Normals	Above	19	18.5	15	11	
	Below	10	10.5	8	12	
Non-schizophrenics	Above	18	7.5	8	7	
	Below	10	9.5	10	11	
Chi-square	..	$\chi^2=4.09$ (d.f.=2) non-significant	$\chi^2=5.06$ (d.f.=2) $.05 > p > .01$	$\chi^2=4.82$ (d.f.=2) non-significant	$\chi^2=9.58$ (d.f.=2) $p < .01$	

* Only 26 schizophrenics, 23 normals and 18 non-schizophrenic patients were included in self-description part of the experiment.

The pronouns used by the subjects were then classified into those that referred to the self as subject ("I") and self as object ("me", "myself", "my" etc.). The two raters working independently and without knowledge of the identity of the subjects performed the classifying. The reliability between the raters in classifying pronouns was indicated by a Rho coefficient of .91 ($p < .01$).

The results of this classification are summarized in Table III.

TABLE III
Number of "I" and "Me" Self-references

		Part A		Part B	
		"I"	"me"	"I"	"me"
Median count per subject		1.5	1.5	0.5	1.0
Schizophrenics	Above	15	25	7	7
	Below	20	10	19	19
Normals	Above	17	19	8	15.5
	Below	12	10	15	7.5
Non-schizophrenics	Above	6	10	6	10.5
	Below	11	7	11	6.5
Chi-square of distribution of three groups		$\chi^2 = 2.76$ (d.f. = 2) non- significant	$\chi^2 = 9.66$ $p < .01$	$\chi^2 = 0.47$ (d.f. = 2) non- significant	$\chi^2 = 9.26$ (d.f. = 2) $p < .01$

The table shows that the three groups did not differ significantly in number of subject pronouns ("I") used. However, the schizophrenics used significantly fewer object pronouns ("myself", "me", "mine", etc.) than either normals or non-schizophrenic patients. This occurred in both Parts A and B of this study. The differences are highly significant when tested by median test.

Study 2: Naming of Body Parts

As the previous study had been strictly empirical in that no hypothesis had been formulated beforehand, it was decided to conduct another experiment with a different procedure. The method involved pointing to various parts of the patient's body and asking him each time, "What is this?". The parts used were the subject's (a) right hand, (b) left ear, (c) right foot, (d) shirt, (e) nose and (f) ankle. All the answers were recorded verbatim. The subjects were 32 schizophrenic patients, 31 normals, and 10 non-schizophrenic patients. The score was the number of times each subject mentioned the pronoun "my" before he named the part to which the experimenter pointed. The hypothesis was that the schizophrenic group would use fewer "my" or "me" responses than the normal or non-schizophrenic patient groups. The differences were tested by median test. The results are summarized in Table IV. The results disclosed, as predicted, that the schizophrenics gave significantly fewer "my" responses than the other groups. The schizophrenics were more likely to respond "a hand" or "the hand" while the normals would respond "my hand".

TABLE IV
Possessive Pronouns Used in Naming Body Parts

						Number of "my" Responses per Subject	
						Above Median	Below Median
Schizophrenics	..	..	..	..	..	7	25
Normals	..	..	..	..	..	22	9
Non-schizophrenics	..	..	..	..	..	6	4

$$\chi^2=13.60 \quad p<0.01$$

Thus the hypothesis has been confirmed by an independent experiment using new samples.

Study 3: Who-are-you Test

The subjects used here were 30 schizophrenic patients and 29 normal controls, all of whom were employees of the hospital (mostly in the non-professional category, although a few social workers and book-keepers were included). The responses to the question, "Who are you?", were scored according to the categories given by Bugental (10) and are presented in Table V. The only differences occurred in the categories of sex and occupation.

TABLE V
Responses to Question "Who are you?"

Response Category						Normals N=29	Schizophrenics N=30
Name	..	..	..	..	..	22	22
Personal pronoun	..	..	..	..	..	4	2
Person, human being	..	..	..	..	..	6	8
Sex	..	..	..	..	..	20	10*
Age	..	..	..	..	..	3	1
Occupation	..	..	..	..	..	19	3†
Family status	..	..	..	..	..	9	5
Residence	..	..	..	..	..	2	3
Nationality, religion	..	..	..	..	..	4	2
Appearance	..	..	..	..	..	0	2
Patient	..	..	..	..	..	0	3
Miscellaneous	..	..	..	..	..	1	8
Don't know	..	..	..	..	..	0	6

* Difference between groups significant at 5 per cent. level ($\chi^2=7.42$, $p < .01$).

† Difference between groups significant at 1 per cent. level ($\chi^2=19.73$, $p < .01$).

*Study 4: Drawing of Missing Parts in Mirror**

This study was purely empirical, although a general hypothesis was formulated that the drawing of the bodily parts not seen in the mirror will correspond more accurately to the real parts of the body in the normals and the non-schizophrenics than in schizophrenics. The following measures of the drawings were used as indices: (1) head, longitudinal, (2) head, transverse, (3) hand, longitudinal, (4) hand, transverse, (5) width of the shoulders. The measurements were correlated with corresponding real measurements of the body. In none of the groups were the correlation coefficients significant. Therefore, the hypothesis was neither proved nor disproved. When the sizes of the body parts in the drawings made by each group were compared, it was found

* Twenty-six schizophrenics, 30 normals and 11 non-schizophrenic patients participated in this study. Apart from one normal, these subjects were used in the previous study.

that the schizophrenics drew smaller hands than did the normals or non-schizophrenic patients. It was first thought that the difference was one of proportions. However, subsequent analysis of the data indicated that this difference was one of absolute sizes. The schizophrenics drew heads and shoulders the same absolute size as the control groups, but drew smaller hands. The statistical significance of this finding was tested by analysis of variance, the results of which are summarized in Table VI.

TABLE VI
The Mean Measurements and Summary of Analysis of Variance

			Mean Measurements				
Diagnosis			Hand Longi- tudinal	Hand Trans- verse	Head Longi- tudinal	Head Trans- verse	Shoulders
Schizophrenics	..	..	9.7	4.9	19.3	17.4	31.7
Normals	..	..	13.6	6.7	20.4	17.8	35.4
Non-schizophrenics	..	..	12.9	6.7	17.8	16.8	34.2
Between							
Sum of (d.f.=2)	..	..	215.0	49.9	60.3	8.2	197.1
Squares within (d.f.=64)			1388.2	236.5	1034.8	802.7	3062.5
and d.f.							
Total (d.f.=66)	..	..	1603.2	286.4	1095.1	810.9	3259.6
F-ratios			4.96	6.75	1.86	0.33	2.05
			p>.01	p>.01	n.s.	n.s.	n.s.

F-ratios of the measurements of the drawings of the head and of the shoulder are not significant. The F-ratios of the measurements of the drawing of the hand are significant at 1 per cent. level.

The results of "t" tests for the differences between the mean measurements of the drawings of the hand are summarized in Table VII.

TABLE VII
The "t" Tests of the Differences of the Measurements of the Hand Drawings

			Longitudinal		Transverse	
Groups			Difference of Means	"t"	Difference of Means	"t"
Schizophrenics-normals	..	..	3.9	3.12 p<.01	1.8	3.53 p<.01
Schizophrenics-non-schizophrenics			3.2	1.92 .1>p>.05	1.8	2.61 .05>p>.01
Normals-non-schizophrenics	..	..	0.7	0.42 n.s.	0.0	0.0

It can be seen from Tables VI and VII that the differences between the measurements of the drawings of the hand between the schizophrenic group and the two other groups are statistically significant.*

Thus the empirical finding was that schizophrenics draw statistically significantly smaller hands than normals and non-schizophrenics. There is a possibility that this may be due to a change in the perceived body (body image), schizophrenics perceiving distal parts of their body smaller. Thus their body image shrinks, as it were, on the periphery.

* One "t" ratio falls short of 5 per cent. level, but one has to remember that the non-schizophrenic group was very small.

Study 5: Draw-a-person Test

No differences between the groups could be found with this test.

Study 6: Left-Right Discrimination

There was no difference between the three groups in this procedure. This result does not support the idea of Angyal (3) that the schizophrenic experiences a "vague uncertainty" in distinguishing between right and left.

Study 7: Size of Extremities

In addition to the previous studies, a seventh study was carried out some time later. As it did not involve the mirror, the method used and the results will be described together. This study was designed to test a hypothesis derived from the fourth study. In that study it was found that schizophrenics drew statistically significantly smaller hands than normals and non-schizophrenics when they were asked to draw the upper part of their body in natural size. It was thought that this might be due to a change in the perceived body and that the schizophrenics perceived distal parts of their bodies smaller than normals and non-schizophrenics. As this study was purely empirical, it could not be used as a proof of a *post hoc* hypothesis. A new experiment was set up to test this hypothesis that schizophrenic patients perceived their own hands and feet smaller than controls.

METHOD

Photographs were taken of a young man's left hand and left foot, both from dorsal aspects. Fifteen prints in various sizes were made of the hand and foot photographs. The longitudinal sizes of the hands and feet obtained on the prints are reproduced in Table VIII in centimetres.

TABLE VIII
Sizes of the Photographs in Centimetres

Hand	..	2.4	5.1	8.0	10.4	12.3	13.6	14.5	15.7	16.7	19.2	21.0	23.9	25.2	30.1	34.5
Foot	..	2.0	6.5	7.9	10.1	14.1	16.9	18.4	20.0	21.5	23.0	24.5	26.0	27.6	32.0	35.0

It can be seen that apart from the extreme ranges, the steps by which the sizes of the photographs increased were approximately 1 cm. for the hands and 2 cm. for the feet.

In order to secure a uniform background, the hands and feet were cut out from the prints and glued on green cardboard rectangles 14 inches×22 inches in size. They were displayed on a stand, the height of which could be adjusted according to the subject's height. The stand was placed against a wall, which was covered with green paper (the same shade green as the cardboard rectangles). This was done in order to produce a homogeneous background and to minimize any effect of the contrast between the size of the rectangle and the size of the photograph. Another stand with a chin support was placed in front of the first stand. The height of the second stand could also be adjusted according to the subject's height. A sheet of green cardboard was attached to the two stands screening off the rest of the subject's body when he placed his chin on the chin support. The subject was instructed to stand in front of the chin support, put his hands behind his back, place his chin on the chin support and look straight ahead at a red dot in the centre of the stand on which the photographs were to be placed. The stands were so adjusted that the red dot was level with the

eyes and the viewing distance was 30 cm. The following instruction was read to the subject: "We shall show some pictures of hands. For each hand we want you to tell us whether it is larger, smaller, or the same size as your own hand." It was stressed that it was the size of the photograph and not the size of the hand originally photographed which was to be compared. Each subject was shown both an ascending and descending series, the sequence of which was varied according to a predetermined random order. A standard neon light was used for illumination.

When the photograph was changed, a green shield was placed in front of the patient's eyes to prevent him from catching a glimpse of the experimenter's hand. On each presentation the subject was asked whether the picture of the hand was larger, smaller, or the same as the size of his hand. The ascending series of presentation was shown until the subject made three consecutive judgments that the photograph was larger than his own hand. The descending series was shown until the subject made three consecutive judgments that the photograph was smaller than his own hand. The subject's score was the mean size of the pictures judged the same size as the subject's own hand in both ascending and descending series. (In cases the subject's judgment changed from larger to smaller without any judgments of equality, the mean size of the two pictures at the point where the judgments changed became the subject's score.)

The same procedure was followed with the photographs of feet, with the subjects having to compare the sizes of the photographs with the sizes of their own feet. There was a short break between the series for the subject to rest a few minutes.

The design of the experiment was controlled for the order of presentation of the ascending and the descending series. There were four orders of presentation:

1. Hand ascending, hand descending, foot ascending, foot descending.
2. Hand ascending, hand descending, foot descending, foot ascending.
3. Hand descending, hand ascending, foot ascending, foot descending.
4. Hand descending, hand ascending, foot descending, foot ascending.

In each group an equal number of subjects was assigned to each order of presentation.

In the second part of the experiment the subject was taken to another room where he stood 22 inches in front of a semicircular rod at a height level with the subject's eyes. On this rod were hung 12 brown men's socks which varied by equal steps from size 7 to size 13. Each sock enclosed a cardboard frame which preserved the shape of the sock. Each sock was marked by letters from A to L, printed on paper discs of the sizes proportional to the sizes of the socks. The subject was instructed to look around and to tell, without touching the socks, which one was closest to the size of sock that would best fit him. At the end of the experiment, the longitudinal size of the subject's left hand and foot was measured by two independent observers.

SAMPLE

As the photographs showed a male hand and foot, only male subjects were used. The sample consisted of three groups: 20 schizophrenics, 20 normal subjects, and 20 non-schizophrenic psychiatric patients. The schizophrenic sample included only patients in whom the diagnosis of schizophrenia had been

firmly established by all psychiatrists who had examined them. Six patients were diagnosed as hebephrenic, three as catatonic, two as paranoid, two as simple, and seven as undifferentiated schizophrenics. The mean age was 39.5 years (S.D.=7.5). The average length of stay in the hospital was 11.7 years (S.D.=6.0). No patient in whose case there was a possibility of mental deficiency or organic brain disease was included. No patient undergoing insulin or electrical shock treatment was included. Only patients who would co-operate in the experiment were included in the sample. The normal group included 20 men who were either workmen or members of the hospital maintenance staff. They were the same social and educational background as the patients and they were paid for participation in the experiment. Their mean age was 34.1 years (S.D.=11.1).

In the non-schizophrenic patient psychiatric group, ten patients were diagnosed as alcoholic, five as psychopathic personality, two as epileptic, one as depressive, one as sexual deviant, and one as a case of situational maladjustment. Their mean age was 37 years (S.D.=13.0). The average length of stay in the hospital was 9 months (range from 3 days to 7 years). In all three groups it was made certain that the subjects understood the instructions. No subjects with gross visual abnormalities were included. If a subject used glasses, he was told to wear them during the experiment.

RESULTS

The pictures were judged as to whether they were larger, smaller or the same as the subject's own hands or feet. Therefore, the judgments depended on the real sizes of the subject's own hands and feet. Taking this into consideration, an analysis of co-variance was carried out in which the mean sizes in centimetres of the pictures judged the same as the subject's own hands and feet were adjusted to the real sizes of hands and feet. The significance of the differences between these adjusted measures was tested by "t" tests.

The results are summarized respectively for the hands in Tables IX, X, and XI, and for the feet in Tables XII, XIII, and XIV.

TABLE IX

Correlations Between Real and Estimated Hand Sizes

			Mean Real Size	Mean Estimated Size	Correlation
Schizophrenics	..	..	18.9	17.5	$r = .48$ (.05 p .01)
Normals	..	..	19.1	21.2	$r = .31$ (n.s.)
Non-schizophrenics	..	..	19.0	21.5	$r = .47$ (.05 p .01)

TABLE X

Variance Table for Hand Estimates

Source of Variance			Sum of Squares of Errors of Estimate	d.f.	Mean Square	F
Total	..	..	616.03	58	—	—
Within groups	..	..	460.19	56	8.21	9.46 (d.f.=2)
Adjusted means	..	..	155.84	2	77.92	p.01

TABLE XI

"t" Ratios for Differences Between Real and Estimated Hand Sizes

Group	Difference of the Means of Estimated Sizes	Adjusted "t" Ratios	P
Schizophrenics-normals ..	3.7	4.08	.01
Schizophrenics-non-schizophrenics	4.0	4.41	.01
Normals-non-schizophrenics ..	0.3	0.33	n.s.

TABLE XII

Correlations Between Real and Estimated Foot Sizes

Group	Mean Real Size	Mean Estimated Size	r (correlation)
Schizophrenics	21.0	20.9	r = .28 (n.s.)
Normals	20.8	23.8	r = .30 (n.s.)
Non-schizophrenics	20.8	24.0	r = .18 (n.s.)

TABLE XIII

Convariance Table for Foot Estimates

Source of Variance	Sum of Squares of Errors of Estimate	d.f.	Mean Square	F
Total	855.41	58	—	—
Within group	725.27	56	12.95	5.02
Adjusted means	130.14	2	65.07	p .01

TABLE XIV

"t" Ratios for Differences Between Real and Estimated Foot Sizes

Group	Difference of the Means of Estimated Sizes	Adjusted "t" Ratios	P
Schizophrenics-normals	2.9	2.54	.05 > p > .01*
Schizophrenics-non-schizophrenics	3.1	2.72	.01
Normals-non-schizophrenics	0.2	0.17	n.s.

* When one-tail test is used, this "t" ratio has $p < .01$.

From the tables it can be seen that all the differences are in the predicted direction and are significant at 1 per cent. level. (The differences in foot estimation between the normal and schizophrenic group is also at the 1 per cent. level when a one-tail test is used, which is a legitimate procedure because the differences were predicted by the hypothesis.) Thus the results quite clearly confirm the hypothesis that schizophrenics perceive the distal parts of their bodies smaller than do non-schizophrenic controls.*

As in the experiment two series of presentation were used—ascending and descending—there was a possibility of "anchor" effect. The "anchor" effect is due to the fact that the judgment of size does not depend only on the size of

* Similar results could be obtained when non-parametric statistics were used. It was found that schizophrenics significantly more often chose as the same pictures which were smaller than their hands and feet. The normals and non-schizophrenics tended to choose as the same pictures bigger than their hands or feet. The differences between the groups were tested by Chi-square test. The differences between the schizophrenics and the two other groups were in the predicted direction and highly significant. The Chi-square for the hand judgments were 10.0 and 14.5 ($p < .01$) and for the foot judgments, 5.6 and 4.0 ($p < .05$).

the particular object judged but also, in accordance with Helson's adaptation level principle, on the sizes of the objects which were estimated earlier in the series. Thus in the ascending series there would be a tendency for the subjects to estimate the smaller sized hands as equal to their own hands and feet, and would judge a larger size in the descending series. The difference between the size in the ascending series and the size in the descending series estimated the same as the subject's hand or foot constitutes his "anchor effect". Salzinger (50) has shown marked "anchor effect" in weight judgments of schizophrenic subjects. In our experiment, all the groups showed some "anchor effect" and it was slightly more pronounced in the schizophrenic group. However, the difference failed to reach statistical significance. The schizophrenic subjects also judged a greater number of pictures as being the same size as their hands and feet, but the difference was again not significant.

As far as the second part of the experiment was concerned, it was predicted that the schizophrenic subjects would choose smaller size socks than the controls. There was a slight trend in the predicted direction which, however, was not even near being statistically significant. The range of the choices made by the schizophrenic patients was much narrower than that of the other subjects. This could be accounted for by a positional set (the schizophrenic subjects did not look around) or lack of interest in the experiment. However, in the first part of the experiment it was found that there was a significant correlation ($r = .48$) in these patients between the real sizes and estimated sizes of the hands. This suggests that the schizophrenic patients were co-operating and were not making random choices anyway in the first part of the experiment.

The other possibility could be that the second task was much more concrete than the first one and, therefore, easier for schizophrenic subjects. Also, all the socks were displayed at the same time and the choice of "an average", neither too big nor too little, sock in the middle could have been influenced by the adaptation level. The latter could be more effective when the stimuli are displayed simultaneously than when they are displayed in succession. Be that as it may, the results of the first part of the experiment establish the validity of the hypothesis beyond any doubt.

In order to find whether there was a relationship between the sizes of the chosen socks and the sizes of the photographs judged the same as the feet, correlations between the two sets of sizes were calculated. Correlations were also calculated between the sizes of the chosen socks and the real sizes of feet. These correlations as well as the correlations between the sizes of the photographs and the sizes of feet, calculated previously, are reproduced in Table XV.

TABLE XV
Correlations of the Sizes of Feet, Socks, and Photographs

Groups				Judged Size (photos) and Socks Choice	Sock Choice and Real Size	Judged Size (photos) and Real Size
Normals	..	..	..	.34	.63	.30
Non-schizophrenics	..	..	..	.12	.11	.11
Schizophrenics	..	..	..	.13	.28	.28

One can see from the table that all correlations are positive. However, only the correlation between the sizes of chosen socks and the real sizes of feet is statistically significant, and this only for the normals.

DISCUSSION

These experiments indicate that in schizophrenia both body image (perceived body) and self concept are changed. In the studies of body image it was found that schizophrenics perceive distal parts of their body smaller than normal controls and non-schizophrenic patients. One possible explanation deriving from the theories of Schilder and Federn is that for schizophrenic patients there is a narrowing of the self boundary with the distal parts of the body being less ego-involved, less cathected, and, therefore, less valued. Bruner and Goodman (9) have shown that children judge valued objects as larger than non-valued objects. Raush (47) has shown that this tendency is even more marked in schizophrenic patients. Thus the fact that schizophrenics tend to draw distal parts of the body small and to underestimate the size of these parts may be due to their lower valuation of their bodies and, therefore, lesser ego-involvement. If one accepts the idea often reported in literature that the ego or centre of oneself is located in the head, we would expect this loss of ego-involvement to be more marked on the periphery of the "physical" ego. The size of the distal parts would therefore be underestimated. However, an explanation of the impaired body image according to libido theory conflicts with Schilder's (53, 54) interpretation of Freud's theory of schizophrenic regression. This interpretation, accepted by Fenichel and others, maintains that the schizophrenic withdraws libido from objects and concentrates it toward his own body. If this is so, we should expect the schizophrenic to be at least as accurate as normals in estimating the sizes of body parts. We might predict that the schizophrenic would tend to *overestimate* the size of body parts, which certainly was not our finding.

There is another explanation which, in the opinion of the authors, is of greater heuristic value and would better satisfy the principle of economy of hypotheses. One can attribute these abnormalities of body image in schizophrenic patients to a breakdown of size constancy and distortions in perception of space. Weckowicz (58) and Crookes (15) have shown that in schizophrenic patients, size-constancy is poorer than in control groups. Weckowicz *et al.* (59, 60) have also shown that distance constancy in these patients is poorer than in control groups. The perceived space of schizophrenic patients lacks in depth. The sizes of the objects are seen more in accordance with their visual angle, because distance is taken less into account than it is with normal people. Distal parts of the body will, therefore, be perceived smaller in relation to the parts near the eyes. It was found that schizophrenics under-estimated the sizes of their hands and feet in comparison with the control groups. If size constancy explanation is true, this difference should be even more pronounced in the case of the feet than in the case of the hands. This is because the hands are customarily nearer to the eyes than are the feet. Thus the perception of feet should be more affected by a breakdown in size constancy than the perception of hands. The results of the experiment have not borne it out. However, the photograph of the foot was somewhat ambiguous in that the heel was missing because the photograph had been taken from above. This could have been a source of confusion for many subjects. Some of them could have made allowance for the missing heel and some could have not. Another experiment with a less ambiguous foot photograph would be indicated. Another possible explanation is that in humans, the cortical area representing hand is much larger than that of foot. Therefore, one would expect the image of hand to be much better developed and differentiated than the image of foot. Since in any generalized pathological process

of the cortex higher differentiated functions are affected earlier than less differentiated functions, the part of the body image representing hand will be more affected than the part of the body image representing foot. Thus there may be a secondary factor modifying the effects produced by the impairment of size constancy alone.

If the "size-constancy" explanation is tentatively accepted, there are intriguing possibilities concerning the relationship between perceived body and perceived space. Since Lotze (36) put forward his "local sign" theory of space perception, there has been a lot of speculation regarding the relationship between bodily sensation and space perception. Most theories of space perception, particularly those of empiricist tradition, explain space perception as being due to association between visual sensations and proprioceptive sensations. An example of such theory is Freeman's Motor-Adjustment Theory (22). This author emphasizes motor posture or set of the organism at the time of stimulation. The "proprioceptive backlash" from the muscles and joints indicates what is to be done with the perceived object and, therefore, what movements are necessary to reach them in space. According to these theories the individual learns about space by exploration. During this exploration he moves around and proprioceptive sensations resulting from these movements and changes of bodily posture become associated with visual percepts. The literature on child development is replete with such accounts. Gesell (25) attaches great importance to the eye-hand co-ordination and co-operation in the infant in his exploration of surrounding space. Piaget (44) attributes the earliest cognitive "schemata" to these early manipulations and eye-hand explorations. The earliest system of spatial co-ordinates is related to body image. Left-right, up-down, in front and in the back, are judged from the point of view of the body position. It is only towards 9-10 years that an independent system of spatial co-ordinates is developed (45). The space directly surrounding the body, particularly the region between the hands and eyes, and around the orifices, is structured first. The farther regions are structured later. Von Uexküll (57) has compared the perceived three-dimensional world to a soap bubble. This "soap bubble" grows larger as the child matures.

More recently some theorists of Gestalt and, therefore, nativist orientation have recognized the importance of body image in space perception. The most striking example is the "Sensory Tonic" field-theory put forward by Werner and Wapner (63). These authors have found that the co-ordinates of perceived space depend on stimulation of the muscles. If this stimulation is not symmetrical, there is a compensatory deviation in the co-ordinates of perceived space.

Neurological investigations also indicate that perception of space is closely related to perceived body. Gerstmann (27) has shown that damage to the dominant parietal lobe produces finger agnosia, acalculia and left-right disorientation. He pointed out that in finger agnosia the knowledge of the manipulatory space round the fingers is affected. Macdonald Critchley (14) in his recent monograph on parietal lobes indicated a close relationship between disturbance of body image (atopognosia, anosognosia) and the disturbances in space perception and orientation and, also, apraxia. In milder cases where space perception and orientation is disturbed, only the third dimension in the perception of depth is affected. (The subject can copy a two-dimensional drawing but finds it difficult to draw or to build three-dimensional figures.) It is obvious that perceived body is closely related to the perception of space and that both of them are related to the function of parietal lobes. Hallucinogenic drugs such as lysergic acid, mescaline, bufotonin and others produce both distortion of the

perceived body and the perceived space. Hoffer (31) has found that adrenochrome (another hallucinogenic substance) affects the perception of space and the perception of the parts of the body. His subjects stated that their hands appeared smaller while they were under the influence of the drug.

Disorders of perceived body in schizophrenia are well known. Some of the descriptions made by clinicians indicate quite clearly that these disturbances are related to constancy of perception and perception of space. Bleuler (8) gives the following descriptions of body image distortion occurring in schizophrenia. "The hallucination of bodily sensations present such kaleidoscopic multiplicity that no description could possibly do justice to them . . . The patients are beaten and burnt, they are pierced by red-hot needles, daggers or spears; their arms are being wrenched out; their heads are being bent backwards; *their legs are being made smaller*; their eyes are being pulled out so that in the mirror it looks like they are entirely out of their sockets; *their heads are being squeezed together*; *their bodies have become like accordians being pulled out and then again pressed together.*"* The changes of the perceived body described by this author are exactly the changes one would expect in a case of poor size and shape constancy, with the appearance of body parts changing size and shape with each different distance and angle of viewing. One can postulate a close relationship between constancy of perception, the perceived body and perceived space. Angyal (3, 4) makes the interesting point that sometimes the schizophrenic experiences a reduction or elimination of a third-dimension to his body. He cites several such reports of patients: "Nothing is behind my chest, I have no back"; "I feel flat like those signs on the road"; "I feel so thin that clothes hang on to me, like a skeleton."

In infancy and early childhood the development of constancy of perception helps to form a stable body image, moving and oriented in a three-dimensional space. In schizophrenia, drug-induced psychoses and organic damage to the parietal lobes, the physiological mechanisms controlling these functions are affected. With schizophrenia, in comparison with parietal lobe damage and drug-induced psychoses, the impairment is usually mild but, nevertheless, sufficient to colour the "Weltanschauung" of the schizophrenic.

In the area of self-concept the most outstanding finding concerns self-references. The schizophrenic patients gave a smaller number of self references than the control groups when the subjects were describing themselves or naming parts of their bodies. This indicates that their self-concept, when compared with that of controls, is more limited. Their bodies are less ego-involved. Self is poorly delineated and less structured. As has already been mentioned, the emergence of self is a social process. Freud (23), Mead (38), and more recently, Cameron (11), Coutu (16), and Parsons and Bales (42) have postulated that the development of self involves some kind of "internalization" process of the early objects of social interaction. The attitudes and characteristics of significant figures are somehow internalized and become functional directive systems within the individual. This is the idea behind Freud's concept of "super-ego", Mead's concept of the "generalized other" and Parsons and Bales' view that self is a kind of "mirror-image" of the social relationships the individual has experienced. In the view of the authors of this paper, the "internalization" theory, although describing to some extent the socialization process, is inadequate to explain some essential aspects of the development of self. It is important that, together with the socialization process, identification with or internalization of certain

* Our italics.

social values, goes another process, namely the emergence of the individual as a self-conscious independent entity in the matrix of social relations. This is achieved by the ability of the individual to perceive the mutuality, complementarity and reciprocity of social roles and expectations. To put it simply, it is the ability to see oneself, as it were, through the eyes of other people. Piaget (43) has shown that the language and thought in small children are egocentric. The ability to see the other's point of view develops only gradually. This is the most important aspect of "role-taking" described by Mead and "role articulation" described by Cameron (11, 12). This being so, there is an intriguing possibility that the emergence of self may depend on the development of a stable body image and, therefore, on more general cognitive processes, like constancy of perception and the ability to form concepts. The ability to interact in a social situation may depend in the first place on the ability to perceive oneself and others as stable phenomena, having certain continuity in time. Constancy of perception implies the ability to perceive an object, as it were, from more than one point of view in space. In shape constancy it involves "seeing" the object simultaneously at several angles. In distance constancy it involves "seeing" the object simultaneously from several distances. To put it in physiological terms, the stimulus pattern received at a certain point of space is integrated with the traces (memories) of the stimulus patterns received at different points of space. There is a close relationship between points of space and the perceived aspects of an object. This relationship forms an invariance which is responsible for the formation of percept-concept of an object. This awareness of more than one aspect of an object, more than one point of view from which it can be observed, is the essence of perceptual constancy. It may also be the essence of the ability to perceive oneself from outside as a separate object or entity. There may be the same basic mechanisms involved in the perception of stable objects related to each other in space, perception of one's body as a stable object, and perception of other people. The role-taking, role-playing, and other aspects of social relationships may be an abstraction of relationships between perceived human bodies, as geometry is an abstraction of relationships between physical bodies. The roots of the physical and social spaces may be the same. In the fundamental and earliest social interactions, the individual's body is actually the chief participant. One could mention as an example the relationship between the infant and his mother. It is largely a bodily relationship depending on handling and bodily contact.

Koffka (34) has pointed to another factor apart from the social factors which may be responsible for the organization of ego in relation to body image. He has stressed the importance of the coincidence between visual and kinaesthetic perceptions. The visual perceptions of the bodily parts are assimilated into the kinaesthetic perceptions of these parts and, therefore, are perceived as different from the outside objects. A new gestalt emerges which has an ego character and which is responsible for the subject's calling his hand "my hand" and his leg "my leg", etc. This new gestalt is called the ego system.

A very important aspect of self is its boundary. It has been investigated by Fisher and Cleveland (21) who maintain that the definiteness of the self boundary depends on the structuring of relations with early social objects. If the relations were well structured and clear-cut, then the self boundary is well defined and clear-cut. If these relations were poorly structured and vague, then the self boundary is poorly defined and vague. One can see again that it is the complementarity and reciprocity of social roles which is very important. A well-structured social relationship is a relationship where the roles, and, therefore,

their complementarity and reciprocity, are clearly defined. There is a distinct and clear "interface"* between the two reciprocal roles. It allows the individual to "see" himself from the vantage point of the other without losing his identity. Sociologists refer to this as role-taking which is distinct from role-playing in that the latter refers to the individual's ability to fill certain social roles, e.g. policeman, student, etc. (cf. Coutu). The role of the individual and the roles of the others are kept distinct and are not confused. A stable body image, which is clearly defined and separated from a stable outside world, is very important in bringing about well-defined social relationships and social roles. Therefore, it is also important in bringing about a well-defined and clearly delineated self.

In the schizophrenic patient constancy of perception is poor. Objects are poorly defined and lack stability. This applies also to this patient's own perceived body and the perceived bodies of other people. Their social roles and relationships are poorly defined; there is no clear-cut reciprocity and complementarity. The subject may be confused in role-taking and role-playing. The self is poorly defined and delineated. The boundary between self and the external world is loose and may disappear altogether. The individual while looking at himself through another's eyes in the process of role-taking may lose his identity. He may literally identify himself with the other. The autobiography of one former mental patient recounts how a patient he knew was unable to keep his feet distinct from his partner's during a dance. He would continually refer to other people's feet as his own. This could account for some delusions of personal identity. It could also account for phenomena of passivity (*automatisme supérieur*). In this condition the subject feels that he no longer controls his thoughts or his body, and that they are controlled by outside forces. Further, it could account for *hallucinations du double* of the French authors ("autoscopy" of the English authors) in which the subject has an hallucination of another person and recognizes this person as himself. It could also account for the phenomena occurring in LSD and mescaline intoxication when the subject sees his own body from outside. Thus, the disorders in the perceived body (body image) and self-concept can be reduced to a disturbance of perceptual constancy occurring in the subject's phenomenological space, which includes both the perceived physical space and the perceived social space. This would make it unnecessary to use the concepts of "projection" and "introjection" which, from the epistemological point of view are not very satisfactory.

Regarding the details of the self-concept studies, it was found that schizophrenic patients when asked, "Who are you?" significantly less often used sex and occupation in their self-description than the other groups. This is again due to a poorly defined self-concept. It supports the frequent references in the literature to poor sex identification of schizophrenic patients. The paucity of answers referring to occupation may be due to the effects of disculturation, a secondary symptom of mental illness, caused by incarceration in a mental hospital.

Another interesting finding was that although schizophrenics less often used self references than the other groups, it affected only the "me" aspect of their selves and not the "I" aspect. In order to speculate on the meaning of this finding, a philosophical digression may be necessary. The Cartesian dualism maintains that both subject and object are primary and irreducible data of experience. The Kantian idealism maintains that the experienced object is created by the subject. If we take the position repudiating both these views and

* We are indebted to Mr. F. Huxley for this term.

side ourselves with the empiricist tradition of philosophy, we will accept sensory experience as the only primary datum. This position was most forcibly put forward by James (33) as "Radical Empiricism" and also by Mach (37) as "Experiential Positivism". Phenomenologists studied the immediate experience called by Husserl (32) "pure being". It was regarded by them as the ultimate reality. More recently, Russell (49) has expressed similar views. The essence of this position is that sensations are neutral, neither matter nor mind, neither object nor subject. These primary sense data, because of certain regularities of occurrence, are classified either as material "things" of the external world or as "contents" of mind. The external world and mind, or object and subject, are, therefore, only secondary logical constructs from the primary sense data. They are frames of reference for what James has called the "neutral stuff" of experience.

This primary polarity of experience has crystallized in the tradition of Western metaphysics into a highly philosophical antinomy of "mind and matter" or "subject and object". In an unsophisticated form it may occur quite early in life with the primary differentiation of experience into "I" and "not I". It is well known that small children have difficulty in distinguishing imagery from perception, dreams from reality. Next, a segment of the "not I" becomes differentiated. This segment of the external world has a special relationship to "I", perhaps on account of the fusion of the somaesthetic with other sensations. This is the perceived body. It is interposed between "I" and the external world. The "me" appears only later as a result of social interactions with other people. Thus in schizophrenic regression the perceived body and the "me" aspect of self may be affected before the "I" aspect. Whether this "I" aspect of self is ever affected in very sick patients is an open question which might be answered by experimentation.

The last point which has to be discussed is the relationship of the perceived body and self-concept to the perception of the external world. Freeman's Motor-Adjustment theory of perception has already been mentioned. According to this theory the motor posture or set through the proprioceptive backlash gives meaning to the perceived objects. In a recent paper, Gerstmann (28) expresses the same views. He states that "Every new set of afferent impressions in order to serve the orientation and recognition . . . must be brought into proper functional relation with mechanism of body image by the activity of the brain before it rises into consciousness. . . . Without that relation the peripheral sensory impression results in an isolated perception accompanied by a feeling of estrangement and isolation from the body." In schizophrenic patients this may take the form of unreality of feelings or of world destruction delusions. There is some evidence (Weckowicz and Blewett (61) and also Crookes (15)) that schizophrenic perception is literal and lacks the same depth of meaning that it has for normals. In these patients, therefore, a vicious circle is set up. Poor constancy of perception leads to the lack of stability of the perceived objects and of the subject's own perceived body. The objects are lacking in meaning or their meaning is distorted. This is aggravated by the fact that the body image to which the percepts of objects are referred is poorly differentiated. The distortion of object perception affects the perception of the subject's own body and the distorted perception of the subject's own body distorts further the perception of objects. This may be related, as suggested by Eickhoff (18), to the impairment of abstract thinking which would agree with the finding of Weckowicz and Blewett (61) that in schizophrenic patients there is a positive correlation between size constancy and abstract thinking.

The impairment of abstract thinking would affect in its turn the formation of self-concept.

Thus, there is a close relationship between the perception and knowledge of the external world, of one's body, and of one's self. One influences another. All three are affected in schizophrenia probably by a disturbance of some underlying physiological mechanism.

SUMMARY

Body image and self-concept were studied experimentally in schizophrenic patients, normal controls and non-schizophrenic psychiatric patients. Seven experimental studies were conducted.

It was found that:

1. Schizophrenic subjects when compared with non-schizophrenic controls underestimated the size of the distal parts of their bodies.
2. Schizophrenic subjects used self-references less frequently than non-schizophrenic controls when they described their bodies.

The theoretical implications of these findings for the body image and self-concept of schizophrenic patients are discussed.

A hypothesis is put forward which relates the perception of one's body and self-concept to constancy of perception and perception of space. A concept of phenomenological space which embraces both physical and social space is tentatively put forward.

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A CONTROLLED TRIAL OF THIOPROPAZATE DIHYDROCHLORIDE (DARTALAN), CHLORPROMAZINE AND OCCUPATIONAL THERAPY IN CHRONIC SCHIZOPHRENICS

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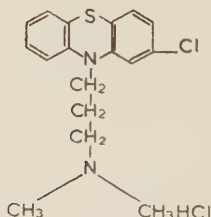
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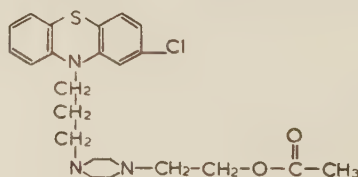
SINCE the introduction of chlorpromazine for the treatment of mental illnesses a number of other tranquillizing drugs, belonging to the phenothiazine group, have come into use. Experience has shown that the first of a new kind of drug is not necessarily the best and it is important that "variations on a theme" should be properly tested.

In 1956 Cusic, Hamilton and Lourie synthesized thiopropazate dihydrochloride (Dartalan) in the Chicago Laboratories of G. D. Searle & Co. Ltd. As can be seen, this drug has a close structural relationship to chlorpromazine.

Chlorpromazine



Thiopropazate



After extensive tests in animals and later in human subjects, thiopropazate was considered to exert tranquillizing effects comparable to those of chlorpromazine. Furthermore, it was found that these effects were produced in considerably lower doses with minimal unpleasant side-effects and a marked absence of toxic reactions. It was studied particularly in relation to toxic effects on the liver and so far no cases of liver damage resulting from its use have been reported. In fact, thiopropazate had been administered to patients who had previously developed jaundice from chlorpromazine, without further ill effects.

A trial of thiopropazate dihydrochloride was made by Edisen and Samuels (1958) on a heterogeneous group of 104 patients with emotional disorders. A double-blind technique was employed with the patients serving as their own controls. Doses of thiopropazate varied from 10 to 120 mg. daily. The patients were assessed for 12 symptoms on a 5-point scale, and improvement was rated in four degrees: Worse, unchanged, slight and definite improvement. An overall estimate was also made. The majority of the patients were schizophrenics and they reported that of 62 chronic schizophrenics treated, 30 showed a definite improvement and of 19 acute schizophrenics, 11 showed definite improvement, particularly in defect of association, depersonalization and anxiety, delusions, withdrawn sociability, flattened affect and anorexia, as compared with those having placebo. Statistical tests were significant at levels $\cdot 01$ and $\cdot 05$ probability.

A number of unpublished observations indicated that thiopropazate might be useful in agitated states associated with cerebral arteriosclerosis. It was effective in cases of catatonic and paranoid schizophrenia, where, in addition to amelioration of mood, there was reported to be improvement in social behaviour and aptitude for work. Other workers reported improvement of hallucinations, delusions and inappropriate affect in chronic schizophrenics, and diminution of psychomotor activity.

It appears to be agreed so far that thiopropazate is three to five times more potent than chlorpromazine and the acute toxic dose is one and a half to four times that for chlorpromazine. Unpublished observations indicate that the therapeutic oral dose range is small, the action of the drug rapid and the full therapeutic effect achieved within one week.

THE PRESENT TRIAL

Many difficulties appear in the evaluation of the effects of a drug on chronic mental patients, especially schizophrenics. It is generally agreed that such patients benefit to a marked degree from changes in environment, increased occupational activity and the promotion of social interaction, Bickford (1955), Merry (1956). Account must therefore be taken of the social and psychological effects produced by the trial itself (Mitchell, 1956). The patients who receive a placebo in order to serve as a control group, themselves benefit from the changed atmosphere of the ward, and this tends to obscure the effects of the drug on the treated group. There is no easy solution to this problem.

Instead of trying to eliminate the effects of environmental influences, it is possible to change the viewpoint of the trial and to attack the problem from the opposite direction. The trial could be designed to determine the effects of a drug combined with occupational and social therapy. Since it is now recognized that tranquillizers have no fundamental effect on the underlying pathology of schizophrenia, it is likely that their greatest value may lie in potentiating the effects of intensive social therapy. In this enquiry, an attempt has been made to tackle this problem, as well as to test the direct value of drug treatment.

POPULATION

The investigation was made on 54 chronic male schizophrenics (average age 38 years), all of whom had been resident in the hospital for a continuous period of not less than two years (average duration of residence in hospital 8.6 years). They were all liable to be overactive and aggressive from time to time. All of them had been referred to the Occupational Therapy department at some time but had not been able to continue to attend because they were too

difficult to control. As a group, they were typical of the patients to be found in a refractory or semi-refractory ward of a mental hospital. Nearly all of them had had courses of E.C.T., over half of them had received insulin coma treatment, and all had had courses of tranquillizer drugs. All drug treatment was discontinued for one month before the first assessment in the trial.

The trial was designed in the form of a 2×3 factorial experiment. The patients were randomly allotted to 6 groups of 9 patients each. Three groups were randomly selected to attend Occupational Therapy (O.T.). They attended the O.T. department on five afternoons a week for 2 hours and were offered a choice of activities varying from simple repetitive tasks to complex, intricate work requiring planning, patience and skill. The patients were encouraged to persist in their chosen tasks or attempt ones requiring more skill, but where necessary they were advised on the activity most suited to their abilities. Each of these three groups was randomly coupled with another group, and the names of the patients in the three pairs of groups given to the hospital pharmacist. He randomly selected one pair of groups to receive chlorpromazine, 300 mg. daily; another group to receive thiopropazate 30 mg. daily, and the third pair of groups to receive placebo tablets. Since two drugs were being administered, it was necessary to have two sets of placebo tablets. One of the groups in the pair receiving placebos had five patients given the placebo tablets matching chlorpromazine and four patients given the placebo tablets matching thiopropazate. The other group of nine patients received the placebo tablets with the numbers reversed. Thus from the point of view of the patients, nurses, and physicians, there were 27 patients receiving one kind of tablet and 27 receiving the other kind, but only the pharmacist knew which of the patients were receiving active and which inert tablets. All the tablets were sugar-coated and the placebo tablets were indistinguishable from the active drugs.

ASSESSMENT

The patients were assessed on Behaviour in the ward by the charge nurses, and on Symptoms by the physicians. Before the trial began, the physicians practised rating patients comparable with those who were to be included in the trial. Each patient was seen at an interview by two physicians, one of whom conducted the interview and the other asked any supplementary questions he considered necessary. The ratings were made independently and then compared. The results were discussed in order to clarify interpretation and to eliminate differences in standards of rating. The charge nurses also made practice assessments on patients not included in the trial, and these were discussed with the physicians. Their ratings were based on the patients' behaviour during the previous week.

All the patients on the trial were then assessed by the physicians at such double interviews, and the ratings summed to give a measure of the patient's condition. The drug trial was then started, and two weeks later the assessments were repeated. They were again repeated 6 weeks later, i.e. 8 weeks after the start of the trial. It was arranged at the second and third assessment, that the patients were not interviewed by the physician in direct charge of them. The difference between the ratings made at the first and second interviews measured the change in the patient's condition after two weeks, and the difference between the ratings at the first and third interviews measured the change in 8 weeks.

As there were two day shifts, there were two charge nurses to each ward. These charge nurses made independent ratings of the behaviour of the patients

in the week preceding the start of the trial, again after two weeks and again after another 6 weeks. The forms on which the ratings were made were collected as soon as they were filled in. The ratings of the two charge nurses were summed to give an assessment of the patient's condition, and changes were measured by subtraction, as described above.

The nurses used a specially designed rating scale for behaviour in the ward, consisting of eight items. This scale is very simple compared with many well-known behaviour rating scales. We consider that a balance has to be struck between the loss of information in a short and simple scale, and the many errors of a long and elaborate one.

The physicians used a scale which was based on a modification of the relevant items in the scale of Lorr (1953). These modifications were made because of difficulties found in interpretation of certain items. Each item was scored from 0-3, for increasing intensity of symptoms. There is no doubt that the use of the scale requires not only practice in the scale, but also experience in interviewing chronic schizophrenic patients. Much patience is needed to persuade withdrawn schizophrenics to talk, and the interviews cannot be hurried. Important information sometimes appeared only towards the end of the interview, for which reason, a set time for the interview is unsatisfactory. It was found convenient to have some knowledge of the patient's history, symptoms and behaviour, in order to have suitable starting points for the interview.

RESULTS

1. *Nurses' Ratings of Behaviour in the Ward*

There is no great difficulty in studying the results of this trial as it affected the behaviour of the patients in the ward. Each nurse rated the patient on eight variables, at the beginning of the trial, after two weeks and again after another six weeks. The nurses' ratings were summed to give a total rating. The difference between the totals at the start of the trial and after two weeks measured the improvement during the first two weeks; and the difference between the first and third ratings measured the improvement over eight weeks (Table I, p. 44). There were six groups of nine patients and the total improvement for each group is given in the appropriate cell of the table.

At the end of two weeks, the patients receiving thiopropazate had a mean improvement of 3.2 points, those receiving placebo had improved by 1.6 points, whereas those receiving chlorpromazine had worsened by 0.6 points. The differences between these figures were statistically significant. The results support the claim that the effects of thiopropazate are manifest in a short period of time.

Occupational therapy also showed its effects quickly. The patients who received O.T. improved 2.7 points, whereas those who did not improved by only 0.1 points. The difference between these two means was significant. It is necessary to point out, however, that O.T. is not possible under "double-blind" conditions, for manifestly *all* the patients knew who was receiving O.T., i.e. those receiving it and those not so privileged, as well as the nurses. It is therefore quite proper to argue that the improvement recorded is merely an expression of the bias of the nurses. The point will be considered again.

At the end of eight weeks, the differences between the mean scores of improvement of the patients on drugs was still significant. Thiopropazate maintained its lead with a mean improvement of 4.6 points, compared with chlorpromazine 1.1 points and placebo 1.0 points. The results of O.T. changed.

TABLE I
Improvement in Ward Behaviour
After 2 Weeks

	Chlor- promazine	Thio- propazate	Placebo	Total
Occupational therapy ..	2	39	33	74
No occupational therapy ..	-13	19	-3	3
Total	-11	58	30	77
Sum of squares = 1,054				

After 8 Weeks

	Chlor- promazine	Thio- propazate	Placebo	Total
Occupational therapy ..	4	44	35	83
No occupational therapy ..	15	39	-17	37
Total	19	83	18	120
Sum of squares = 1,397				
(Each cell gives the total points of improvement for 9 patients)				

Analysis of Variance (2 Weeks)

Source	d.f.	54 × SS	54 × MS	F	P
Drugs	2	7,226	3,613	4.56	< .05
Occupational therapy ..	1	5,041	5,041	6.37	< .05
Interaction	2	722	361	< 1	N.S.
Error	48	37,998	792		
Total	53	50,987			

Analysis of Variance (8 Weeks)

Source	d.f.	54 × SS	54 × MS	F	P
Drugs	2	8,322	4,161	4.52	< .05
Occupational therapy ..	1	2,116	2,116	2.30	N.S.
Interaction	2	6,434	3,217	3.50	< .05
Error	48	44,166	920		
Total	53	61,038			

Those receiving it had a mean improvement of 3.1 points, and those who did not 1.2 points. The difference between these means was not significant statistically.

If the improvement in the O.T. patients is merely a record of the bias of the nurses, it becomes difficult to explain why this bias should have diminished to statistical non-significance by 8 weeks. It is very likely that the patients given O.T. do improve in their general behaviour, and that this improvement appears quite rapidly; hence the result at the end of two weeks. Little further improvement occurs in them, but it can be seen that further improvement has occurred in those not receiving O.T. and it could be suggested that this is the result of the improvement in the general "atmosphere", a sort of "social contagion" of improvement. This is plausible in the light of clinical experience, and has the support of the work by Robin (1957). Detailed examination of the results shows that another interpretation can be made, for it will be observed that the patients receiving neither drugs nor O.T. have in fact worsened, changing from a mean of -0.3 to a mean of -1.9. Most of the improvement is to be found in those patients on chlorpromazine only, who have improved from a mean score of -1.4 at 2 weeks to 1.7 at 8 weeks, supplemented by the further improvement of those on thiopropazate from 2.1 points to 4.3 points. Thus, the patients not receiving O.T. show a continued improvement with the drugs.

At the end of 8 weeks, the disappearance of the main effect of O.T. is accompanied by the appearance of an interaction between drugs and O.T. Of the patients receiving placebo, those on O.T. improved by a mean of 3.9 points, those without O.T. worsening by 1.9 points. For those on thiopropazate, the changes were 4.9 and 4.3 points respectively, and for those on chlorpromazine, 0.4 and 1.7 respectively. It would therefore appear that the drugs tend to inhibit the effects of the O.T., this effect being more prominent with chlorpromazine than with thiopropazate. The presence of such an interaction makes any conclusions about main effects insecure, e.g. that chlorpromazine is no better than placebo, but the number of cases is insufficient for reliable comparisons to be made between individual combinations of treatments.

2. Physicians' Ratings of Symptoms

The improvement scores for the Symptoms were obtained in the same way as those for behaviour in the ward, but the analysis and interpretation of the results were anything but simple. For various reasons (see Appendix), the symptoms were divided into two groups P and N, which were considered

TABLE II
Improvement in P Group of Symptoms
After 2 Weeks

	Chlor- promazine	Thio- propazate	Placebo	Total
Occupational therapy ..	69	55	45	169
No occupational therapy ..	19	74	127	220
Total	88	129	172	389

Sum of squares=7,869

After 8 Weeks

	Chlor- promazine	Thio- propazate	Placebo	Total
Occupational therapy ..	80	40	46	166
No occupational therapy ..	58	112	123	293
Total	138	152	169	459

Sum of squares=8,431

(Each cell gives the total points of improvement for 9 patients)

Analysis of Variance (2 Weeks)

Source	d.f.	54 × SS	54 × MS	F	P
Drugs	2	10,586	5,293	1.08	N.S.
Occupational therapy ..	1	2,601	2,601	<1	N.S.
Interaction	2	26,154	13,077	2.68	N.S.
Error	48	234,264	4,880		
Total	53	273,605			

Analysis of Variance (8 Weeks)

Source	d.f.	54 × SS	54 × MS	F	P
Drugs	2	1,446	723	<1	N.S.
Occupational therapy ..	1	16,129	16,129	3.72	< .05
Interaction	2	18,662	9,331	2.15	N.S.
Error	48	208,356	4,341		
Total	53	244,593			

TABLE III
Improvement in N Group of Symptoms

				After 2 Weeks			Total
				Chlor-promazine	Thio-propazate	Placebo	
Occupational therapy	..			57	15	89	161
No occupational therapy	..			15	—18	24	21
Total				72	—3	113	182
Sum of squares=4,096							

				After 8 Weeks			Total
				Chlor-promazine	Thio-propazate	Placebo	
Occupational therapy	..			22	17	48	87
No occupational therapy	..			10	5	25	40
Total				32	22	73	127
Sum of squares=3,761							

(Each cell gives the total points of improvement for 9 patients)

				Analysis of Variance (2 Weeks)				
Source	..	..	d.f.	54 × SS	54 × MS	F	P	
Drugs	..	..	2	20,762	10,381	3.41	< .05	
Occupational therapy	..		1	19,600	19,600	6.44	< .05	
Interaction	..	..	2	1,634	817	<1	N.S.	
Error	..	..	48	146,064	3,043			
Total				188,060				

				Analysis of Variance (8 Weeks)				
Source	..	..	d.f.	54 × SS	54 × MS	F	P	
Drugs	..	..	2	4,382	2,191	<1	N.S.	
Occupational therapy	..		1	2,209	2,209	<1	N.S.	
Interaction	..	..	2	242	121	<1	N.S.	
Error	..	..	48	180,132	3,753			
Total				186,965				

separately. The N group consists of the expression of various delusions, together with evidence for hostility; and the P group consists of disturbances of speech and thought, disturbances of posture and mannerisms, disturbed affect, including apathy, and finally, objective evidence for hallucinations based on the patient's behaviour rather than on his statements. The P group of symptoms describes the withdrawn uncommunicative patient, with whom an interview is a continuous struggle to make contact and to elicit some response. Such patients are not "out of contact" with their environment, but their response to it has undergone a qualitative change from the normal. The patient who shows the N group of symptoms responds to the interview in normal fashion, answering questions more or less freely, and giving vent to his delusions.

There was a general tendency for all symptoms to diminish at successive interviews. For the P group, at the end of 8 weeks the only significant difference

was between those patients on O.T., who improved by a mean of 6.1 points, and the rest, who improved by a mean of 10.9 points. The same but smaller trend was found at 2 weeks, and it is of interest that the patients on O.T. showed the same score at 2 and 8 weeks, the change being due to the continued improvement in the patients not on O.T. Although no other differences were significant, at both the second and third assessments the patients receiving placebo improved most, and those receiving chlorpromazine improved least.

Turning to the N group of symptoms, we found the reverse effect, for here at 2 weeks the patients on O.T. showed a mean improvement of 6.0 points, compared with the 0.8 points of improvement shown by the rest, and this difference was statistically significant. The drug effects were also statistically significant, with the patients on drugs doing worse than those on placebo; the results were an improvement of 2.7 points for those receiving chlorpromazine, a worsening of 0.1 points for those on thiopropazate, compared with an improvement of 4.2 points for the patients receiving placebo. At the end of 8 weeks, the same trends were visible, but all the differences had diminished below statistical significance. The general conclusion was that for the N group of symptoms, all the patients in the trial were recorded as having shown an improvement, but that neither drugs nor O.T. had made any significant difference in the end, although in the first two weeks the patients on O.T. had made a temporary spurt ahead of the others.

The results for all symptoms can be found by adding the results for the P symptoms to those of the N symptoms. Since O.T. and the two drugs show opposite effects for the two groups, when these are added, they cancel out, and the nett effect is that there are no significant differences due to drugs or O.T. either at 2 or at 8 weeks*.

TABLE IV
Decrease in Scores on Bipolar Factor

After 2 Weeks				
	Chlor- promazine	Thio- propazate	Placebo	Total
Occupational therapy ..	12	40	-44	8
No occupational therapy ..	4	92	103	199
Total	16	132	59	207

Sum of squares=7,083

After 8 Weeks				
	Chlor- promazine	Thio- propazate	Placebo	Total
Occupational therapy ..	58	23	-2	79
No occupational therapy ..	48	107	98	253
Total	106	130	96	332

Sum of squares=8,496
(Each cell gives the total change for 9 patients)

* The sum of squares for the total symptoms is 17,447 at 2 weeks and 15,888 at 8 weeks. The analysis of variance can be calculated from this plus the information available in Tables II and III.

TABLE IV—*continued*

				Analysis of Variance (2 Weeks)			
Source	..	..	d.f.	54 × SS	54 × MS	F	P
Drugs	..	..	2	20,634	10,317	2.01	N.S.
Occupational therapy	..	..	1	36,481	36,481	7.12	< .01
Interaction	..	..	2	36,650	18,325	3.58	< .05
Error	..	..	48	245,868	5,122		
Total	..	..	53	339,633			

				Analysis of Variance (8 Weeks)			
Source	..	..	d.f.	54 × SS	54 × MS	F	P
Drugs	..	..	2	1,832	916	< 1	N.S.
Occupational therapy	..	..	1	30,276	30,276	4.92	< .05
Interaction	..	..	2	21,192	10,596	1.72	N.S.
Error	..	..	48	295,260	6,151		
Total	..	..	53	348,560			

DISCUSSION

The ratings described above are based on measurements of individual items in the scales, and therefore a good deal of information is available on qualitative changes in the patients, not necessarily related to "improvement". These have been omitted from the above account of results, in order to avoid obscuring the aim of the investigation, which was primarily concerned with the effects of treatments in improving the patients' illness. These qualitative changes are dealt with below, together with their theoretical background.

It is now generally agreed that the phenothiazine compounds alter the behaviour of chronic schizophrenic patients, but have little or no effect on the underlying pathological process. The results of this investigation are in agreement with this opinion, the drug effects being significant on behaviour in the ward but not significant on Symptoms at interview. The former merit close scrutiny. The most striking result, in a sense, is the absence of any significant difference between the effect of chlorpromazine and placebo. It cannot be argued that the method of assessment of behaviour was incapable of showing any improvement, because the thiopropazate showed a significant one, and so did the O.T.

It is possible that the length of the trial was insufficient. However, favourable results with chlorpromazine were reported by Seager (1955) in a controlled trial lasting only 4 weeks. Elkes and Elkes (1954) reported that the effects of chlorpromazine were manifested in 3–6 weeks. These are but two examples. It may be that the dose of chlorpromazine was insufficient, but Seager gave only up to 225 mg. daily. Vaughan and Leiberman (1955) reported favourable results in a controlled trial, using 150–200 mg. daily, and Elkes and Elkes used only 150 mg. daily, and reported improvement.

The literature on chlorpromazine is immense, but the number of controlled trials on chronic schizophrenics is relatively small, and of this number some report negative results, e.g. Hall and Dunlap (1955), Mitchell (1956), Little (1958), Fleming and Currie (1958), Walsh, Walton and Black (1959). The present findings of no improvement in symptoms following the administration of chlorpromazine is therefore not an isolated one. Nevertheless, the presence of marked inhibitory interaction between this drug and O.T. makes conclusions about the general effect insecure.

The upshot of our work with the scale used is that we are not satisfied

that the interview is an adequate method for obtaining full information about the symptoms of chronic schizophrenic patients. Also we believe that ratings on ward behaviour are by themselves insufficient for making an assessment of the patient's condition, i.e. the state of his illness.

The interaction between drug and O.T. on behaviour is one of peculiar interest. Grygier and Waters (1958) found that patients on an energetic re-socialization programme improved more when given chlorpromazine than when given placebo. The improvement was slight but statistically significant. The present results are that the drugs inhibited the effects of O.T. but this became manifest only after several weeks. It is true that none of the patients of Grygier and Waters were deprived of O.T., but it is difficult to see how this would affect the results. It is clear that further investigation will be necessary to resolve these discrepancies. If the present result is confirmed, the implications would be that, in any programme of intensive rehabilitation for chronic schizophrenics, the maximum value of tranquillizing drugs would be at the start.

It is worth recording that, on consulting the ward records after the trial, it was found that one patient receiving chlorpromazine had shown side-effects. He developed symptoms of Parkinsonism, but these disappeared in a few days after the dose was reduced, and did not return when the dose was increased again.

SUMMARY

A controlled investigation was designed to determine the relative values of a new drug thiopropazate dihydrochloride, chlorpromazine hydrochloride and occupational therapy on overactive and aggressive chronic schizophrenics.

Fifty-four patients were randomly allotted to six groups of nine. Three groups attended O.T. and three did not. The pharmacist allocated the two active drugs and similar placebos to paired groups from the O.T. and non-O.T. groups. This information he did not release until the end of the trial.

The patients were rated on their behaviour in the ward by the two charge nurses, and for symptoms by any two physicians not directly in charge of the patient. Practice ratings were made on a similar category of patient beforehand. The ratings were made before the treatments started, after 2 weeks and again after 8 weeks of treatment.

Results:

1. Behaviour in the ward was significantly improved by thiopropazate at the end of 2 weeks and 8 weeks. O.T. significantly improved ward behaviour in the first 2 weeks, but by 8 weeks the other patients had improved sufficiently to make the difference non-significant. Interaction between drugs and O.T. showed that at the end of 8 weeks both chlorpromazine and, to a lesser extent, thiopropazate exerted a significant inhibitory effect on the improvement due to O.T.
2. In the course of the trial, all groups of patients showed improvement in their symptoms, regardless of the combinations of treatment they received. This emphasized the importance of proper control groups in investigations on the effects of treatment.
3. For the P group of symptoms (apathy, mannerisms, hallucinations, etc.) the only significant result was that at 8 weeks patients on O.T. did not improve as much as the others.

For the N group of symptoms (hostility, persecutory and other delusions) all groups of patients improved, but differences between groups were not significant at 8 weeks. At 2 weeks, the patients on O.T. were significantly better than the others, and the patients on placebo were significantly better than those on active drugs. These differences were temporary and had fallen below statistical significance by the end of 8 weeks.

For the total of all symptoms, neither O.T. nor drugs made any significant contribution to improvement.

Factors which may have influenced the results are considered. There is evidence to suggest that in a rehabilitation programme for overactive, aggressive, chronic schizophrenics the maximum value of tranquillizing drugs may be obtained from their use at the start of the programme.

There was no evidence of any soporific effect from these drugs given in the doses of: thiopropazate 10 mg. t.d.s. and chlorpromazine 100 mg. t.d.s. At the dosage level stated one patient receiving chlorpromazine developed, temporarily, symptoms of Parkinsonism but no patient receiving thiopropazate showed side-effects.

APPENDIX

THE RESPONSE TO TREATMENT OF A COMPONENT OF CHRONIC SCHIZOPHRENIA

A scale designed for measuring schizophrenia requires a number of items, each measuring a different aspect of the disorder. If the items are all scored in the same way, from normal (absent symptom) to severe symptom, then a normal subject will score zero, and a severely ill patient will score highly on many or all of the items. The sum of the scores on the individual items will tend to be higher for those patients who show more symptoms, and who would therefore be regarded as more ill. It is implicit in such summing, that the items all measure the same thing, more or less.

When two items measure something in common, they will have a common variance, and the scores in them will show a positive correlation. Of course, if they measure opposite aspects of the same quality, they will show a negative correlation. For example, one item may measure an aspect of social adjustment and the other of maladjustment. In such a case, one item will have to be given a negative weight, i.e. its score will have to be subtracted from the other. Which one is given the negative weight depends on whether we are measuring adjustment or maladjustment.

When a set of items is properly designed to measure different aspects of one quality, then the intercorrelations will all be positive. (The reverse is not necessarily true). If the items measure nothing else, i.e. the non-common variance is all error variance, then the matrix of correlations will have its rows and columns proportional; in mathematical terms, it will be of unit rank, and in psychological terms it will have only one factor. In general, it is almost impossible to obtain such a set of items. In the case of schizophrenia, each item is concerned with a specific aspect of schizophrenia, which need not even be present in each patient. The matrix of correlations will therefore have a rank of more than one, i.e. it will have more than one factor.

The first or general factor can be extracted from the matrix of correlations mathematically, leaving residual correlations (strictly, covariances) which can be seen to fall into two groups. These groups are negatively correlated with each other, the items in each group being positively correlated. Such a matrix of residuals contains a bipolar factor (at least one). The first factor can also be eliminated experimentally, by selecting the subjects in such a way that they all have the same score (as much as possible) on the general factor. In order to obtain factor scores for the bipolar factor, one group of items must be given negative weights; and which group is given the negative weights depends on which direction the bipolar factor is measured from.

On turning to the intercorrelation matrix of the physicians' scale for symptoms, it is seen that the correlations fall into two groups, each of which is negatively correlated with the other, the items being positively correlated within the group. The items as designed, should have formed a matrix with all correlations positive, and indeed, it can be said that they would have done so had the subjects interviewed included a sufficient number of mild schizophrenic patients and normal subjects. In the light of the foregoing theoretical analysis, it is evident that intense selection has eliminated the general factor, leaving only the bipolar factor. In effect, the correlation matrix shows that the patients selected for the clinical trial form a homogeneous group of chronic schizophrenics. Despite the bipolar pattern of the correlations, it is meaningful to sum the scores on all the items and to use a diminution of such a total score as a measure of over-all improvement of the schizophrenic symptoms.

A score for the bipolar factor can be obtained by subtracting the scores of the N group of symptoms from the P group. A high score means that the patient tends to show the pattern of the P group (unresponsive at interview, apathetic, bizarre behaviour), whereas a low (or negative) score means that he shows the N group of symptoms (delusions freely expressed, communicative at interview). A decrease in the patient's score does not measure improvement in his condition but a change in his symptoms from the P type to the N type.

The intercorrelations of the items in the nurses' scale for behaviour in the ward are all positive, but not high, the simple average being .44. The conclusion to be drawn from this is that the items all measure ward behaviour as designed, and that despite the homogeneity of the symptoms of the patients, there is considerable variation in their behaviour. To those who are acquainted with the administration of mental hospitals, this is not unexpected. The P group of symptoms correlate positively with the nurses' ratings (P for positive) and the N groups correlate negatively (N for negative).

The foregoing discussion will now have made clear the reason for keeping the two groups of symptoms distinct. It will also have justified the next step, which is to *subtract* the improvement in N scores from the improvement in P scores. The resulting scores do not now measure improvement, but a change from P symptoms to N symptoms. The statistical analysis can be seen in Table IV. The results show that there is a general tendency for the patients to manifest their delusions and hostility, etc., more at the second and third assessment than at the first. This is much greater in those patients not receiving O.T. than the rest. The difference is highly significant after 2 weeks (7.4 points of change against 0.3 points respectively) and less, although still significant, at 8 weeks (9.4 points against 2.9 points). The decrease in the difference between the two groups is largely due to the change in those patients receiving O.T. The drugs do not produce any significant change, but there is significant interaction between drugs and O.T. at 2 weeks, the interaction being of such a nature that the drugs tend to inhibit or reverse this effect. Since the interaction effect has disappeared by 8 weeks, it would probably be wiser to await confirmation of its presence before drawing conclusions from it.

These results are very difficult to interpret. It may be that the interviewers become more skilled at interviewing these patients under these special conditions. It is more likely that the patients are becoming more accustomed to these interviews and responding to them in more normal fashion. In either case, it is even more difficult to understand why such changes, from P to N symptoms, should be inhibited by the experience of O.T. on five afternoons a week. In the circumstances, it is only possible to come to the empty conclusion that the response of chronic schizophrenic patients to the subtle "social" changes produced by a drug trial, including repeated interviewing and O.T., are very complex, and we do not understand them.

NURSE'S RATING SCALE FOR BEHAVIOUR IN WARD

Attitude to work

Normal attitude, co-operative	..	..	..	..	..	..	..	0
Can do simple jobs only	..	..	..	..	..	..	..	1
Requires some supervision	..	..	..	..	..	..	..	2
Needs constant supervision and urging	..	..	..	..	..	..	..	3
Refuses work, passively or actively	..	..	..	..	..	..	..	4

Attention to dress and person

Attends to clothes and appearance normally	..	..	..	..	..	..	0
Dresses himself, but looks untidy	..	..	..	..	..	..	1
Dresses himself, but needs adjustments	..	..	..	..	..	..	2
Requires help to get dressed and cleaned	..	..	..	..	..	..	3
Has to be dressed and washed	..	..	..	..	..	..	4

Relation to other patients

Helpful and friendly, co-operative in activities	..	..	..	..	..	..	0
Occasionally talks or helps others	..	..	..	..	..	..	1
Will talk when spoken to	..	..	..	..	..	..	2
Will only say a word or so	..	..	..	..	..	..	3
Ignores other patients and may strike them	..	..	..	..	..	..	4

Relation to medical and nursing staff

[illegible]

Behaviour at meals

Normal manners and behaviour	0
Peculiar habits and unco-operative with others ..	1
Stealing and snatching food	2
Wolfing and gobbling food, seldom using cutlery ..	3
Requires supervision or encouragement to eat ..	4

Toilet behaviour

Goes normally to lavatory	..	..	..	..	..	..	..	..	0
Requires to be taken or fetched out	..	..	..	..	..	..	..	..	1
Occasionally incontinent	..	..	..	..	..	..	..	..	2
Frequently incontinent	..	..	..	..	..	..	..	..	3
Smearing sometimes	..	..	..	..	..	..	..	..	4

Activity

Normal activity and mobility	..	..	..	..	..	..	..	..	0
Lethargic	Overactive	..	..	..	..	..	..	..	1
Tends to sit about	Restless	..	..	..	..	..	..	..	2
Has to be moved	Never still	..	..	..	..	..	..	..	3
Resistive and Rigid	Rushing about	..	..	..	..	..	..	..	4

Speech

Normal speech and conversation	..	..	..	..	..	..	..	..	0
Taciturn, inconsequential, no real conversation	..	..	..	..	..	..	..	..	1
Says only a few words, or speech disorganised	..	..	..	..	..	..	..	..	2
Occasional mumbles	..	..	..	..	..	..	..	..	3
Mute or incomprehensive speech	..	..	..	..	..	..	..	..	4

PHYSICIAN'S RATING SCALE FOR CHRONIC SCHIZOPHRENIA

Adapted from the M.S.R.P.P. (Lorr Scale)

- P. 1. How direct and relevant are his responses to questions or to the topic discussed?
 0 Direct and relevant.
 1 Somewhat rambling and tangential.
 2 For the most part irrelevant.
 3 Wholly irrelevant.
- P. 2. Does he assume or maintain peculiar, unnatural or bizarre postures?
 0 None
 1 For short periods
 2 Throughout most of the interview
 3 Throughout the entire interview.
- P. 3. Are his thoughts consistent with his mood, or is there a discernible lack of harmony between them?
 0 Consistent.
 1 A little disharmonious.
 2 Distinctly disharmonious.
 3 Appear totally unrelated.
- P. 4. Does he exhibit any repeated peculiar gestures, grimaces or mannerisms?
 0 None.
 1 Occasionally.
 2 Fairly frequently.
 3 Throughout the interview.
- N. 5. Does he tend to suspect or to believe on slight evidence or without good reason that people and external forces are trying to or now do influence his behaviour and control his thinking?
 0 No unjustified suspicion.
 1 Inclined to suspect.
 2 Believes others are trying to control him.
 3 Believes he is influenced or controlled.
- P. 6. Are the elements of his speech logically consistent and connected by some idea or relationship, or do they tend to be inconsistent and disconnected? (Rate what is most representative during the interview.)
 0 Coherent and consistent.
 1 Slightly incoherent and inconsistent.
 2 Distinctly incoherent and inconsistent.
 3 Conspicuously scattered, disconnected or incoherent.
- N. 7. Does he bear little hostility or a high degree of ill will, resentment, bitterness or hate?
 0 No hostility.
 1 Slight hostility.
 2 Moderate hostility.
 3 Much hostility.

- P. 8. Does he have any insight into his hallucinations? (Score 0 for no evidence of hallucinations.)
- 0 Full insight.
 - 1 Possibly full insight.
 - 2 Some insight.
 - 3 No insight.
- P. 9. How frequently does he speak, mutter or mumble to himself, seemingly to carry on conversations with hallucinatory voices?
- 0 Not at all.
 - 1 Occasionally.
 - 2 Fairly frequently.
 - 3 Throughout the interview.
- P. 10. Is there any evidence that the patient has auditory hallucinations?
- 0 None.
 - 1 Doubtful.
 - 2 Probable.
 - 3 Certain.
- P. 11. Does the patient ever glance up as if listening to auditory hallucinations?
- 0 Not at all.
 - 1 Doubtfully or occasionally.
 - 2 Fairly frequently.
 - 3 Throughout the interview.
- P. 12. Does he repeat certain words or phrases in a meaningless, stereotyped or mechanical fashion?
- 0 Never.
 - 1 Occasionally.
 - 2 Fairly frequently.
 - 3 Almost constantly.
- P. 13. Is his speech irregularly interrupted, halted or blocked for varying periods of time because of difficulty in finding words for his thoughts?
- 0 No speech blocks.
 - 1 A few interruptions.
 - 2 Many interruptions and conversation very difficult.
 - 3 Patient is mute or almost mute.
- N. 14. Does he have an exaggeratedly high opinion of himself, or an unjustified belief or conviction of having unusual ability, knowledge, power, wealth, or status?
- 0 No exaggerated high opinion of himself.
 - 1 An exaggeratedly high opinion.
 - 2 Conviction of unusual power, wealth, etc.
 - 3 Conviction of grandiose or fantastic power, wealth, etc.
- N. 15. Does he tend to suspect or to believe on slight evidence or without good reason that some people are against him (persecuting, conspiring, cheating, depriving, punishing) in various ways?
- 0 No unjustified suspicions.
 - 1 Inclined to suspect.
 - 2 Inclined to believe.
 - 3 Has firm conviction.
- N. 16. Does he tend to suspect or to believe on slight evidence or without good reason, that some people talk about, refer to, or watch him?
- 0 No unjustified suspicions.
 - 1 Inclined to suspect.
 - 2 Inclined to believe.
 - 3 Has firm conviction.
- N. 17. Is there evidence of false ideas or beliefs? If present, are these ideas or beliefs (a) sufficiently plausible as to be accepted by a normal person uninformed as to the facts, (b) implausible but not impossible, (c) impossible or bizarre (e.g. mind controlled by radio waves, heart removed or dead)?
- 0 No evidence of false beliefs.
 - 1 Plausible to the uninformed.
 - 2 Implausible.
 - 3 Impossible or bizarre.
- P. 18. Does the patient's mood and emotional response show blunting?
- 0 Not at all.
 - 1 Slight blunting.
 - 2 Severe blunting.
 - 3 Complete apathy.

*Inter-correlation Matrix of Physicians' and Nurses' Ratings of 54 Male Chronic Schizophrenic Patients
(Decimal points omitted)*

Item No.	Title of Item	1	2	3	4	6	8	9	10	11	12	13	18	5	7	14	15	16	17	1	2	3	4	5	6	7	8
1	Relevant speech	100																									
2	Bizarre postures	1	100																								
3	Inappropriate affect	29	20	100																							
4	Mannerisms	31	19	31	100																						
6	Incoherent speech	85	15	33	32	100																					
8	Insight into Hallucinations	2	12	12	9	13	100																				
9	Talking to voices	26	-6	13	19	29	-2	100																			
10	Evidence of hallucinations	13	14	31	23	18	82	10	100																		
11	Glancing at hallucinations	21	34	34	65	27	23	35	44	100																	
12	Stereotyped speech	49	19	45	28	59	-1	16	17	35	100																
13	Thought blocking	5	57	19	30	16	3	-3	11	26	33	100															
18	Blunting of affect	11	60	13	10	28	9	7	23	31	38	60	100														
5	Ideas of influence	-9	-10	17	-17	-16	22	-13	25	-6	-6	-18	-11	100													
7	Hostility	1	5	-2	-10	-9	-12	-8	-17	-14	-4	-20	-26	3	100												
14	Grandiose delusions	5	-20	6	-20	12	12	-7	-9	-19	-22	-36	38	11	20	100											
15	Persecutory delusions	-3	-18	3	-12	-13	20	-13	17	-9	-9	-23	-33	26	36	23	100										
16	Ideas of reference	-11	-20	1	-29	-19	35	-12	28	-14	-22	-18	-18	49	-3	18	59	100									
17	Implausible delusions	29	-40	19	-7	16	-11	20	3	-3	5	-50	-34	31	27	45	44	30	100								
1	Attitude to work	-9	24	1	-1	5	10	8	15	15	7	27	39	-19	-4	-7	-5	-8	-22	100							
2	Attention to dress	14	29	-16	4	13	14	11	15	10	2	32	39	-11	-15	3	-4	-10	-29	52	100						
3	Relation to patients	5	21	6	8	10	5	12	8	1	9	28	33	-32	13	-10	-2	-30	-20	65	45	100					
4	Relation to staff	10	26	1	13	22	-7	18	-4	17	26	30	45	-25	2	-24	-20	-35	-19	50	36	65	100				
5	Behaviour at meals	9	19	-11	10	11	6	15	7	2	6	35	35	-17	-13	-1	1	13	-33	54	59	54	42	100			
6	Toilet behaviour	27	34	-5	2	25	-14	-6	-1	-4	23	43	47	-29	20	-11	-20	-20	-23	36	49	30	27	38	100		
7	Activity	1	7	4	-8	-7	10	-6	7	3	2	30	16	-16	-11	5	9	-12	-17	36	51	45	28	42	30	100	
8	Speech	8	40	3	26	11	6	10	13	29	16	39	58	11	-3	-18	-31	-29	-33	46	51	41	63	43	19	27	100

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THE BODY CONCEPT

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THE CONCEPT OF THE BODY

THE need to clarify the "confusion in neurology and allied disciplines between the body image, the body schema, the body concept and the perceived body" was emphasized by Smythies (1953). For the neuropsychiatrist it is perhaps the disorders of the body schema and perceived body which are of the greatest interest and importance, but the confusion which still exists between the body concept and the body percept make it probable that a definition and examination of the body concept would clarify thinking about all Body Image problems.

There has, so far, been no adequate definition of what is meant by the term "body concept", and I am indebted to Dr. J. P. S. Robertson whose original critical contribution in Reitman's *Psychotic Art* (1950) stimulated an analysis of the term Body Image, for the following definition. Robertson (1958) suggests as an operational definition of a *concept*, the set of phenomena (a) named by an individual when asked to give the meaning of a word, or (b) listed by him in response to a questionnaire on the meaning of a word, or (c) indicated by his actions in specific choice situations. While concepts vary in complexity and have denotative and connotative aspects, they are given cohesion by the existence of a word as a symbol. We can, therefore, define the *body concept* as the set of phenomena named by an individual when asked to describe the body, reply to a questionnaire, or draw the human figure. This is a *general body concept*. An individual's concept of his own body would be the set of phenomena named by him when asked to describe his own body, reply to a questionnaire, or draw it.

It can be seen that the concept obtained will depend upon, among other factors, the questions which are asked. The instructions "Describe your own body" and "Describe the human body" would almost certainly yield differing concepts. Previous workers have used this technique; for example, Goodenough (1926) instructed children "to make a picture of a man", while Wright (1956), using Eaton's (1940) Semantic Frequency List, asked, in effect, a large group of English, French, German and Spanish literary laymen "How do you describe the body in writing?" A similar method was employed by Tait and Ascher (1955) who asked various groups of people to "Draw the inside of the body including all organs". The effect on the concept of the nature of the instruction was recognized by Tait and Ascher who wondered whether they might have obtained other results if they had instructed their subjects to "Draw the inside of a *person*".

EXPERIMENTAL METHOD

It was decided to compare a body concept in subjects totally blind from birth with the concept of normal and schizophrenic subjects, and so a drawing technique could not be used. A method which might be described as "associative listing" was therefore employed. This is very similar to the technique described by Bousfield and Sedgewick (1944). The subjects were presented with a form at the top of which they were instructed to write their occupation, age and sex in appropriate spaces. In order to reassure them of the anonymity of their contribution to the research, the sighted normals were requested not to put their names on the paper and no note was made of the names of the blind. This was not done in the case of the schizophrenic patients who were given the list with other research material.

Below this there were three columns with the headings reading from left to right "Names of Colours", "Parts of the Body" and "Names of Occupations". Just above the columns was printed the instruction "Under each of the following headings please write down a list of 10 names". No further instructions were given. When, very infrequently, subjects asked for further instructions, as little as possible was said to make the matter clear. Only words listed under the heading "Parts of the Body" were used in this study.

THE SUBJECTS

One hundred and ten adult sighted subjects were examined; 55 male and 55 female. The group consisted of workers at an electronics factory and the clerical and artisan staff of a hospital. Nurses were not tested as it was felt that attendance at lectures in medical subjects might influence the results. In addition 83 patients diagnosed as schizophrenic were tested. There were 46 women and 37 men. All were co-operative patients, the majority of whom had spent many years in hospital. Twenty-nine subjects, totally blind from birth, were also examined. In this case the test was administered individually; the instructions were given verbally and the subjects' replies written down by the examiner. There were only 7 blind male subjects, in spite of the co-operation of various blind organizations to secure more. All the blind subjects tested were Braille readers and any considered to be suffering from a serious emotional disturbance were excluded. In all subsequent discussion the words "blind subjects" refer to subjects totally blind from birth.

THE RESULTS

The Frequency of Mention

The frequencies with which the individual body words occur in the lists obtained from the 139 normally sighted and totally blind subjects have been calculated and are shown in Table I. In this calculation singular and plural forms of the same word have been summed, as have synonyms when they appeared to be coterminous; for example *trunk* and *torso* or *breast* and *bust*. Anatomical terms were not summed with popular words except in the case of *thorax* and *chest* where the equivalence seemed close. The frequencies are shown for sighted normal male and female subjects separately, but for the blind no sex differentiation is made because of the small numbers tested. Only parts mentioned by more than 5 per cent. of subjects are included.

TABLE I

Frequency of Occurrence and Ranks of Body Names in Sighted and Blind Subjects

Name of Body Parts	Blind and Sighted Subjects		Sighted Subjects		Blind Subjects	
	Total Frequency of Occurrence	Rank of Total Frequency	Frequency in Males	Frequency in Females	Total Frequency of Occurrence	Rank of Total Frequency
Arm(s)	113	1	47	49	96	1
Leg(s)	112	2	43	50	93	2
Head	102	3	40	43	83	3
Foot, feet ..	94	4	41	38	79	4
Hand(s)	84	5	35	33	68	5
Finger(s) ..	65	6=	30	25	55	6
Eye(s)	65	6=	26	20	46	7
Nose	63	8	23	18	41	11
Ear(s)	61	9	24	20	44	9
Toe(s)	50	10	25	17	42	10
Neck	49	11	16	29	45	8
Chest, thorax ..	45	12	22	16	38	12
Mouth	31	13	10	10	20	17=
Ankle(s)	29	14=	14	13	27	13
Shoulder	29	14=	12	12	24	14=
Heart	29	14=	7	14	21	16
Knee(s)	28	17	17	7	24	14=
Stomach	25	18	5	13	18	20
Thigh(s)	22	19	7	13	20	17=
Trunk, torso ..	19	20=	9	10	19	19
Lung(s)	19	20=	6	9	15	21
Brain(s)	17	22	6	5	11	23=
Hip(s)	15	23	4	8	12	22
Elbow(s)	14	24=	5	4	9	27
Spine	14	24=	4	4	8	28=
Liver	13	26=	4	7	11	23=
Tooth, teeth ..	13	26=	5	2	7	31=
Kidney(s)	12	28=	4	7	11	23=
Wrist(s)	12	28=	3	7	10	26
Rib(s)	11	30=	4	4	8	28=
Face	11	30=	1	5	6	33
Back	9	32=	2	2	4	35=
Chin	9	32=	4	4	8	28=
Abdomen	9	32=	4	3	7	31=

In Table II those parts named by less than 5 per cent. of subjects are arranged according to their individual frequencies. Seventy-five body parts were named in all. Thirty-four parts are mentioned by more than 5 per cent. and 41 parts by less than 5 per cent. of all examined. No part is mentioned by 100 per cent. of subjects, but arm or leg, which are highest in order of frequency, are listed by about 80 per cent. of subjects. Only 12 body parts are listed by more than 25 per cent. of sighted subjects and 14 body parts by more than 25 per cent. of the blind. The parts listed by the sighted are *arm, leg, head, foot, hand, finger, eye, neck, ear, nose, toe*, and *chest*. The blind list the same parts

TABLE II

*Frequency of Occurrence**Parts Listed by Less than 5 Per cent. of Normal Sighted and Blind Subjects*

Parts Listed Once:	Parts Listed Twice:
Back passage	Appendix
Cheek	Bladder
Collar bone	Bones
Diaphragm	Buttocks, seat
Epiglottis	Forehead
Femur	Humerus
Forearm	Shoulder blade
Hip bone	
Jaw	Parts Listed Three Times:
Knee cap	Throat
Lips	Shin
Nerves	Intestine
Patella	Nail(s) or fingernails
Phalanges	Muscle
Private parts (<i>sic</i>)	
Pupil	Parts Listed Four Times:
Sacroiliac	Waist
Skin	Pelvis
Skull	Breast (or bust)
Spleen	
Tibula (<i>sic</i>)	Parts Listed Five Times:
Thumb	Calf
Temple	Tongue
	Hair

except *neck* which is replaced by *mouth*, while *heart* and *stomach* are added. Comparisons of body parts which are listed significantly more frequently or less frequently by the totally blind from birth in comparison with normally sighted subjects are given in Table V.

Tables III and IV show the word frequencies for the schizophrenic subjects;

TABLE III

Frequency of Occurrence and Ranks of Body Names in Schizophrenic Subjects

Name of Body Parts	Total Frequency of Occurrence	Rank of Total Frequency
Leg(s)	70	1
Arm(s)	62	2
Head	61	3
Foot, feet	59	4
Hand(s)	43	5
Eye(s)	34	6
Ear(s)	32	7=
Toe(s)	32	7=
Finger(s)	31	9
Nose	29	10
Neck	28	11
Chest thorax	25	12
Heart	24	13
Stomach	18	14
Mouth	14	15
Lung(s)	13	16
Knee(s)	12	17=
Shoulder	12	17=
Abdomen	11	19
Hair	10	20=
Thigh(s)	10	20=

TABLE III—*continued*

Name of Body Parts						Total Frequency of Occurrence	Rank of Total Frequency
Tooth, teeth	..	..	..	..	..	9	22
Hip(s)	..	..	..	..	..	8	23=
Muscle(s)	..	..	..	..	..	8	23=
Elbow(s)	..	..	..	..	..	7	25=
Back	..	..	..	..	..	7	25=
Trunk, torso	..	..	..	..	..	6	27=
Spine	..	..	..	..	..	6	27=
Nail(s)	..	..	..	..	..	6	27=
Liver	..	..	..	..	..	6	27=
Rib(s)	..	..	..	..	..	6	27=
Lip(s)	..	..	..	..	..	5	32=
Kidney(s)	..	..	..	..	..	5	32=
Forearm(s)	..	..	..	..	..	5	32=

these are not separated according to sex. In Table III parts mentioned by more than 5 per cent. of subjects are included. Eighty-nine different responses were given. Thirty-four body parts are named by more than 5 per cent. of schizophrenics and 41 parts by less than 5 per cent. Eight responses (occurring only once) are unusual while 6 are irrelevant. Unlike the blind and sighted normal subjects several schizophrenics only listed 3 or 4 words.

A comparison of the lists shows considerable similarity between the schizophrenic and normal subjects. There are, however, some differences but

TABLE IV
Frequency of Occurrence
Parts Listed by Less than 5 Per cent. of Schizophrenic Subjects

Parts Listed Once:	Parts Listed Twice:
Membrane	Skin
Digit	Blood
Ligaments	Chin
Vessel	Biceps
Fat	Bladder
Tibia	Breast
Femur	Flesh
Loin	Body
Uterus	Vein
Limb	
Sole	Parts Listed Three Times:
Groin	Pelvis
Intestine	Waist
Gland	Face
Nerve	Wrist
Sinew	
Appendix	Irrelevant Words:
Heel	Lady(ies) mentioned twice
Cheek	Cuckoo
Throat	Leverett
Buttock	Fox
Artery	Claw
Internal organs	Food
Unusual Responses:	
Right arm	Lower part
Pulse	Upper part
Aural	Right side
Figure	Left side

only *ankle* occurs significantly less frequently in schizophrenics (1 per cent. level) than normals (Table V). There are no other significant differences.

TABLE V

(Comparison of Significant Differences in Total Frequency of Occurrence Between Sighted Normals and Blind Subjects and Schizophrenic Subjects)

Body Parts more Frequent in Blind Subjects

Part	Significance Level (Per cent.)	Rank in Blind	Rank in Sighted Normals
Nose	1	1	11
Eye	5	2=	7
Mouth	5	9	17=
Tooth	5	15=	31=
Back	5	18=	35=

Body Parts less Frequent in Blind Subjects

Leg	5	2=	2
Arm	1	5=	1
Neck	1	22=	8
Trunk	5	Not named	19

Body Parts less Frequent in Schizophrenic Subjects

Part	Significance Level (Per cent.)	Rank in Schizophrenics	Rank in Sighted Normals
Ankle	1	35=	13

No part occurred significantly more frequently in schizophrenic subjects.

Thirteen parts are listed by more than 25 per cent. of schizophrenics. These are the same as for normals with the addition of *heart*.

Order of Mention

The mean relative positions of individual words in the word lists have been calculated for all words occurring more than 5 times in either of the three lists. In Table VI (page 62) these mean ranks together with the rank of the mean ranks are shown.

Frequency of First Mention

Those parts mentioned first in the word lists by both sighted and blind subjects are shown in Table VII (page 63). Significantly more blind subjects mentioned *ear* first and significantly fewer mentioned *head* first. In sighted subjects *head*, *arm*, *leg* and *hand* accounted for 82 per cent. of the cases; in the blind these accounted for 57 per cent. of first mentions, and in schizophrenics for 71 per cent.

Sex Differences

These have only been studied in the sighted normal subjects. Two statistically significant differences were found in the sighted group; *knee* was more commonly listed by men and *neck* by women. One cannot attach much weight to this finding as it was not reproduced with the blind, where proportionately more males mentioned *neck*.

TABLE VI
Order of Mention

Part	Sighted		Blind		Schizophrenic	
	Mean Rank	Rank of Mean Rank	Mean Rank	Rank of Mean Rank	Mean Rank	Rank of Mean Rank
Head	3.0	1	4.3	4=	2.7	1
Arm(s)	3.4	2	2.3	1	3.2	3
Leg(s)	4.0	3=	3.0	2	4.3	5
Trunk	4.0	3=			3.0	2
Hand(s)	5.0	5=	5.0	8	5.6	11=
Knee(s)	5.0	5=			7.1	30=
Neck	5.1	7			5.3	8
Mouth	5.2	8	6.2	12=	6.4	23=
Ear(s)	5.4	9	4.4	6	5.5	10
Eye(s)	5.5	10	4.3	4=	5.9	15=
Nose	5.6	11=	5.4	11	5.8	13=
Calf(ves)	5.6	11=				
Brain(s)	5.8	13=	4.2	3		
Foot, feet	5.8	13=	6.3	14	5.9	15=
Shoulder(s)	5.8	13=	6.2	12=	5.9	15=
Rib(s)	5.9	16			4.0	4
Elbow(s)	6.0	17	8.0	19	5.9	15=
Heart	6.3	18	4.6	7	5.2	6=
Wrist(s)	6.4	19				
Ankle(s)	6.5	20				
Abdomen	6.6	21			6.2	21
Lung(s)	6.7	22=			5.2	6=
Chest (thorax)	6.7	22=	6.7	17	5.8	13=
Thigh(s)	6.8	24			7.1	30=
Finger(s)	6.9	25=	6.6	16	6.9	28
Toe(s)	6.9	25=	6.5	15	6.8	27
Tooth, teeth	6.9	25=	8.3	20	6.0	19=
Chin	7.0	28=				
Spine	7.0	28=	8.5	21	8.0	33
Face	7.2	30	7.4	18		
Hip(s)	7.3	31			5.6	11=
Stomach	7.4	32	5.3	10	6.4	23=
Back			5.2	9	7.3	32
Kidney(s)					5.4	9
Forearm(s)					6.0	19=
Muscle(s)					6.3	22
Hair					6.4	23=
Lip(s)					6.6	26
Nail(s)					7.0	29
Liver					9.2	34

There is also a sex difference in regard to the listing of plurals for body parts, e.g. *eyes* instead of *eye*. Singular words are more common in males, plurals in females and this difference is statistically significant in some items. This may be an idiosyncrasy of the present sample or a definite sex trait, and will require testing in further samples.

DISCUSSION

Just as, in our everyday thinking, we fail to distinguish between bodily experience and description, so in all writings of the Body Image, there is little distinction made between the body percept and the body concept.

TABLE VII

Frequency of First Mention in List of Body Parts

Body Part	Sighted		Blind		Schizophrenic	
	Rank	Frequency	Rank	Frequency	Rank	Frequency
Head	1	46	2=	4	1	39
Arm(s)	2	23	1	8	2	15
Leg(s)	3	12	4	3	4	4
Hand(s)	4	9	5=	2	7=	1
Eye(s)	5	6	5=	2	7=	1
Ear(s)	6=	2	2=	4		
Brain(s)	6=	2	5=	2	7=	1
Finger(s)	6=	2	8=	1		
Mouth	6=	2				
Nose	10=	1			5	2
Toe(s)	10=	1			5	2
Trunk	10=	1			7=	1
Waist	10=	1				
Shoulder blade	10=	1				
Diaphragm ..			8=	1		
Hip bone			8=	1		
Heart					3=	7
Thigh(s)					7=	1
Forearm(s) ..					7=	1
Knee(s)					7=	1
Lung(s)					7=	1
Bladder					7=	1
Brain(s)					7=	1
Artery(ies) ..					7=	1
Nail(s)					7=	1
Face					7=	1

Paper after paper on the Body Image confuses concept with percept and many investigators have tried to demonstrate that changes in human figure drawing parallel changes in bodily perception.

Recent papers by Shontz (1956) and Silverstein and Klee (1958) typify the confusion existing between these two quite different aspects of the Body Image.

Human Figure Drawing and the Body Concept

While the operational definition of the body concept makes it desirable for one to consider the many studies of human figure drawing it should be recognized quite clearly that there is a definite difference between the body concepts obtained by drawing and by "associative listing". It is worthwhile to see what relationship, if any, exists between these concepts. We must consider the three stages in the development of children's drawings described by Lowenfeld (1939); the *pre-schematic*, the *schematic* and the *representational*. In the *pre-schematic* stage the child is searching for a method of presenting form. This is a stage dominated by exploration and experiment with forms and symbols rather than with the developed expression of a concept. In the *schematic* stage the child is expressing in his drawings a concept rather than what he sees, and it is this stage which is of importance for us and which Goodenough (1926) has analysed. The child's schematic drawing is bound to a symbol (Lowenfeld, 1939) and resembles the enumeration of objects (Buehler, 1930); two important features of the body concept, as defined by Robertson (1958). Luquet (1913) and Paget (1932) give illustrations of this and show in this stage how various parts of the body may be put down without any synthesis

into a recognizable whole; "an eye will be placed next to the head, an arm next to a leg" (Fig. 1). It is to this stage that the results of our word listing study could, perhaps, be related. After the mental age of 10 children progress to the *representational* stage in their drawing of the human figure. This is the "realistic" stage of artistic production and may be influenced in certain cases by visual and in others by haptic experiences.

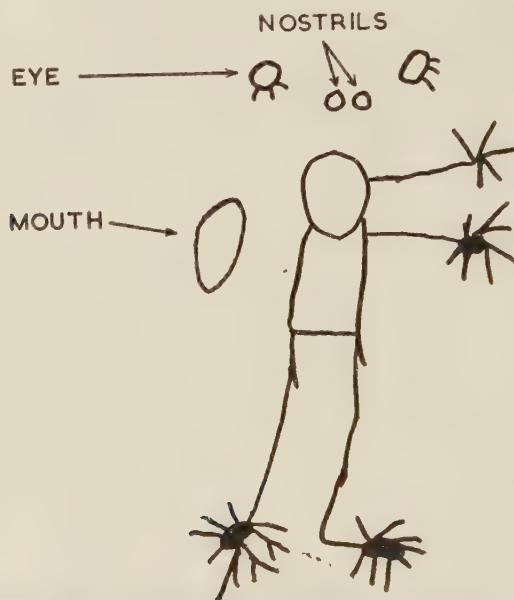


FIG. 1.—Drawing of a man by an East African native girl aged 6 years 6 months.

Representational artistic productions are not related to the body concept in our sense, for the artist does more than list phenomena; he draws on his visual and haptic experience to create form. "The nude is the body re-formed" says Clark (1956) paraphrasing Aristotle's definition of art as that which completes what nature cannot finish. Woëlfli (1932) says this in another way when he states that "all pictures owe more to other pictures than they do to nature".

The "Integral" and "Non-Integral" Parts of the Body Concept

Goodenough pointed out that in its development the child's schematic drawing of the human figure consists of two parts; the first consisting of items which are an integral part of his concept of the object drawn, while the second includes items not yet integrated. "The frequency with which any given characteristic tends to appear is a function of the extent to which it has become integrated into the developing concept." In view of the similarities pointed out between the body concept here described and schematic human figure drawing it is worth considering how frequently a word must occur in the lists before it can be considered to be an "integral" part of the body concept. If from the frequency tables (Tables I and III) one takes those parts listed by at least 25 per cent. of the subjects it is found that the sighted subjects list 12 parts, the blind 14 parts and the schizophrenics 13 parts. These could be considered to represent the "integral" part of the body concept just as the parts which occur

in less than 5 per cent. of subjects can be considered a "non-integral" part of the concept. What of the parts with a frequency of more than 5 per cent. and less than 25 per cent.? There are 21 such parts in the "sighted" list, 20 in the "blind" list and 26 in the "schizophrenic" list, of which 17 parts are common to all lists occurring in roughly the same proportion and order of frequency.

It seems that those parts with a frequency of more than 5 per cent. can be considered to form an "integral" part of the concept, for without them, the concept would be extremely circumscribed and would in any case not include parts considered by Tait and Ascher (Table VIII) to form the "inside-of-the-body" concept nor would it include 5 parts included in the drawings of 25 per cent. of Goodenough's 10-year-old subjects (Table IX, page 66).

TABLE VIII

Rank Order of Internal Body Parts in Different Investigations

Present Investigation		
Sighted	Blind	Schizophrenic
Heart	Heart	Heart
Stomach	Stomach	Stomach
Lung	Brain	Lung
Brain	Spine	Spine
Liver	Lung	Liver
Kidney	Rib	Rib
Rib	Liver	Kidney
Spine	Kidney	Brain
Intestine	Appendix	Bone
Appendix	Bladder	
Bladder		
Spleen		
Tait and Ascher (1955)		
Neuropsychiatric Patients	Naval Academy Candidates	Medical and Surgical Patients
Heart	Heart	Lung
Lung	Lung	Heart
Stomach	Intestine	Stomach
Intestine	Stomach	Intestine
Kidney	Kidney	Kidney
Brain	Liver	Brain
Rib	Brain	Liver
Liver	Oesophagus	Rib
Bladder	Pancreas	Trachea
Vein/blood vessel	Appendix	Bladder
Penis	Trachea	Oesophagus
Testes		Appendix
Trachea		
Oesophagus		
Wright (1956)		
Eaton	Oxford English Dictionary Columns	
Heart	Heart	
Brain	Stomach	
Stomach	Spine	
Womb	Rib	
Rib	Liver	
Lung	Brain	
Liver	Lung	
Bowel	Kidney	
Kidney	Intestine	

TABLE IX

Percentage of Frequency of Occurrence of Body Parts in Children's Drawings of a Man
(after Goodenough)

	7 Year Old Normals						10 Year Old Normals
Head	100						100
Legs	100						100
Trunk	99						100
Eyes	98						100
Nose	95						100
Arms	88						98
Mouth	91						96
Fingers	77						93
Chin and forehead	56						90
Neck	44						83
Feet	53						76
Heel	18						66
Arm joint (elbow or shoulder)	18						64
Hair	22						58
Leg joint (knee)	13						53
Hand	14						48
Shoulders	7						46
Ears	27						36
Nostrils	8						27

This attempt to limit the concept is arbitrary and artificial but is justifiable for the purpose of discussion.

The Determinants of the Conceptual Content

We come now to a consideration of the arrangement of the words in our lists, and the principles according to which they are ordered. We shall consider the effects of perception, motivation, language behaviour and the body schema.

In the schematic drawings of the human figure the child exaggerates the size of items which seem interesting or important; other parts are minimized or omitted. What determines the importance of certain items? The importance of perceptual experience has been stressed by most writers and this view is perhaps best stated by Hobbes when he says, "There is no conception in a man's mind which hath not at first, or by parts, been begotten upon the organs of sense". While direct bodily perceptions can explain much of the conceptual content, it cannot explain the inclusion of parts such as the internal body parts, which cannot be so experienced. Knowledge of these parts depends on less direct or secondary perception; from information in books or pictures or other sources. In the reproduction of these perceptions there is a process of selection. In their drawings children "do not show all the facts which they know about the body but only those which are so essential or characteristic that they occur . . . spontaneously" (Goodenough, 1926). In this selection the individual's mental and bodily constitution, especially such factors as intelligence, sex and social taboos, will operate. Many factors are at work shaping the concept. McKellar (1957) proposes a theory of thinking which summarizes these views. He believes that thought products in general are the result of the organization of previous perceptual impressions. These impressions are provided either by original perceptual content (*the primary perception*) or, by relationships extracted from other perceptual contents (*the secondary perception*), and they are moulded by *motivational factors* which gather together those experiences which are relevant.

The Influence of Primary Perceptions on the Body Concept

The study of the relationship of primary perceptions to the body concept as obtained by associative word listing does not, except in respect of vision, which will be discussed later, yield profitable results. All the parts mentioned except the internal body parts can be perceived by touch or are visible in the individual's own body or in the bodies of others, and it must be assumed, at least for the time being, that their inclusion in the concept could be determined by primary perception. Of the primary perceptions touch, movement, pain and vision could be determinants of the body concept and their possible influence will be considered in more detail.

Since all the parts mentioned (apart from the internal parts) can be touched, it cannot be said that "touchable" parts are more frequently mentioned than "untouchable" parts. On the other hand, some parts frequently touched, for example, *skin, back, chin, hair, forehead* and *lips*, receive scant mention. Closely allied to the manual analysis is the importance of the mobility of body parts. Earl (1933) has stressed that mental defectives draw the head and trunk larger than the limbs since the limbs have less interest for the defective who has "less activity and less interest in activity". Lauretta Bender (1940) studying the body concept of post-encephalitic children by Goodenough's method, found that their concept of their bodies was disrupted by the disturbance of mobility. "It is the most important fact that motor impulses give the final shape to the body image." Schilder (1935) too, feels that the "obedience" of a body organ plays an important part in the creation of the Body Image. Sina Mott (1936) showed that the degree of activity shown in children's drawings of the human figure correlated highly with the child's behavioural activity as rated on the Marston Scale.

All the 5 body parts mentioned by more than half the subjects in the present investigation can be moved voluntarily, as can more than half the parts included in the body concept. The trunk on the other hand is only mentioned by 13 per cent. of subjects, although it comes third in order of mention (Table VI). These findings seem to offer some support for considering the perception of movement a determinant of the body concept.

While Schilder (1935) and Lhermitte (1939) have stressed the influence of pain in the development of the Body Image, consideration of the present list of body parts does not support an influence on the body concept. Those associated linguistically with the suffix "*ache*" such as *head, ear, stomach, tooth* and *back* are scattered in a random fashion throughout the lists. It is possible that pain may have a more direct influence on the development of the body percept and indirectly influence the body concept, but there is no evidence for this view in this experiment.

Vision and the Body Concept

While some of the controversy which has centred on the importance of vision in the body concept can be explained by the failure to distinguish adequately between body percept and body concept, there is, nevertheless, a definite divergence of view on this subject which is not of semantic origin.

Critchley (1953), in a stimulating article on tactile thought in the blind, supports the view of Schilder (1935) and Lhermitte (1939) when he maintains that of the various factors which combine to determine the conception of the body "vision is by far the most important, for it both affords knowledge as to the appearance of one's own body and permits comparison with that of

others. The body image of those *born without sight* must, therefore, be quite unusual". Lowenfeld (1939) studying the drawings of *weak sighted* children found that these were similar to those of normal children and contended that the drawn human schema is not dependent on sight. Riddoch (1941) also denied that the visual image of the body should be given first place and pointed to the expert use of the body by the congenitally blind, while Flugel (1930) points out that civilized man has, apart from the face and hand, little opportunity of observing the bodies of his companions.

From the present investigation, testing as it does the sighted and the totally blind from birth, it is possible to make some suggestions about the part that visual perception plays in the body concept. The internal body parts, depending as they probably do on secondary perception, are almost the same in blind and sighted subjects.

Considering the other parts we find (Table V) that *nose, eye, mouth, tooth* and *back* have a significantly greater frequency of occurrence in the blind. This is represented graphically in Figure 2, where the length of the horizontal

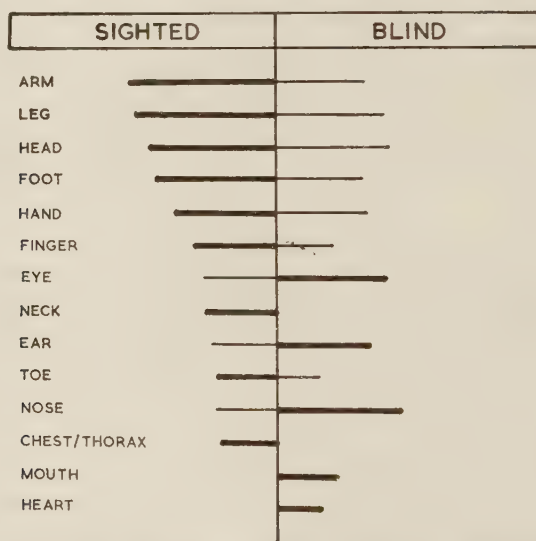


FIG. 2.—Comparison of the frequency of mention of body parts by blind and sighted subjects.

lines denotes the frequency of mention of the first twelve body parts listed by sighted and blind subjects. *Nose* is the most frequently mentioned part in the blind, being mentioned by 75 per cent. of those tested. This finding was unexpected, although a plasticine model of the head by a blind boy discussed by von Stockert (1952) and illustrated in Figure 3 shows a marked exaggeration of the nose. The only other significant difference occurs in the order of the first mention (Table VII) where it can be seen that significantly more blind subjects mentioned *ear* first and significantly fewer mentioned *head* first. There is thus a definite emphasis in blind subjects, with the sole exception of *back*, on facial parts or organs of special sense. The emphasis on the face was not entirely expected as Révész (1950) and Critchley (1953) have stressed the emphasis which the blind place on hands and fingers. Helen Keller's (1908) experiences reinforce this view, for she says, "If I had made a man I should

certainly have put the brain and soul in his finger tips." It is important to remember that Helen Keller was deprived, not only of sight, but of hearing as well.

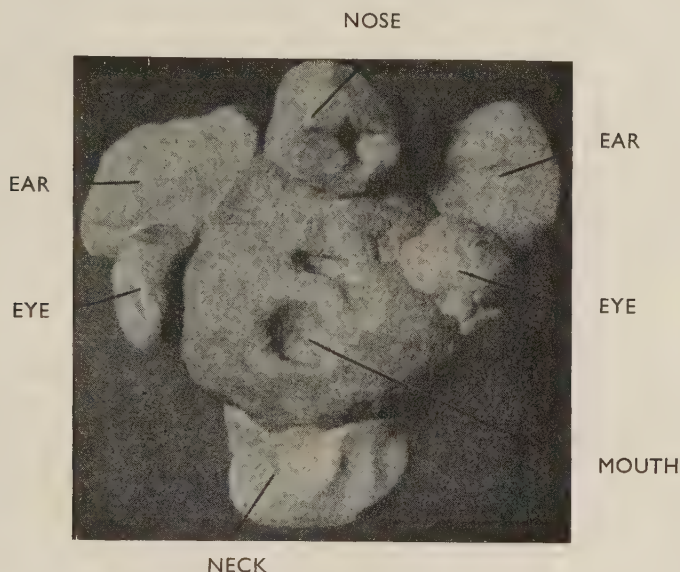


FIG. 3.—A head modelled in Plasticine by an intelligent boy of 12, totally blind from birth. (After Von Stockert.)

For the totally blind who are not deaf, the face and not the hands is of primary sensory importance. The process by which the blind are able to sense obstacles at some distance has been known for some years and has been called "facial vision" by James (1890). One of James's subjects described it thus, "I seem to perceive objects through the skin of my face and to have the impression immediately transmitted to the brain". It has always been suspected that hearing played a great part in this perception and this seems to have been confirmed by the work of Worchel and Dallenbach (1947) since they found that "facial vision" was absent in the deaf blind. For the blind auditory perceptions are apparently referred to the face in the perceived body, and it is of considerable interest to find that the face, presumably as a result of this alteration in the primary bodily perceptions of the blind, assumes a significantly greater importance in their body concept. Similar study of the "deaf-blind" would be of great interest.

The Influence of Secondary Perceptions on the Body Concept

The eight "internal" parts of the body named in Eaton's word frequency lists seemed to Wright (1956) "to differ from all the other named parts in respect of sensory analysis". These parts cannot be perceived directly and our knowledge of them must come from reading, from pictures and from hearsay. They form, nevertheless, an integral part of our body concept resulting from associative listing. They do not appear in the concept delineated by Goodenough's children but they have been shown graphically by the test of Tait and Ascher (1955) where the subjects were instructed to "draw the inside of the body including all the organs". In Table VIII one can compare the rankings of

internal body parts in lists based on the "Inside of the Body Test", drawings of neuropsychiatric patients, naval academy candidates and medical and surgical patients, with the lists of the blind, sighted normal and schizophrenic subjects in the present experiment. The frequency of these words in Eaton's lists and the ranking of the number of columns devoted to these words in the *Oxford English Dictionary* (Wright, 1956) are also given.

If we consider the first eight parts obtained in these eight lists from such widely different sources the similarities are very marked. Five parts are mentioned in all the lists and two in seven of the eight lists. Only five other parts occur. The unanimity not only in content but in ranking and frequency is striking and appears to confirm the assumption that this part of the body concept (about a quarter of the whole concept) is dependent on secondary perception.

Language Behaviour

At this point it is necessary to consider other possible determinants of the "associative listing" body concept which can be described under the heading of language behaviour.

According to the views of the language behaviourists, an individual in the present test situation responds to the stimulus to name 10 body parts by tapping a mental pool of potentially associated words. The selection of words from this pool could be a random matter, or it could be determined by the relative habit strengths of the words. Bousfield and Barclay (1950) support the latter view when they say that "as habits these associates have been subjected to various degrees and types of reinforcement and hence differ in strength". Those responses most extensively reinforced, therefore, are those most likely to occur, i.e. have the greatest frequency. Similarly, habit strength will also determine the order in which the subject draws on the pool of associative responses. In subjects whose verbal habits have been formed in a common culture there should be a positive correlation between frequency and order of mention. Bousfield and Barclay found this positive correlation for their subjects.

In the present study, taking words occurring at least five times in the "sighted normal" lists, a Spearman rank-order correlation of 0.57 between total frequency and mean rank-order of mention, was obtained. Whether it would have been higher in a group whose cultural background was as homogeneous as Barclay and Bousfield's undergraduates is impossible to say.

Zipf (1945, 1949) suggests determinants other than habit strength and by an analysis of samples of written English, Latin and Chinese has shown that the frequency of occurrence of words is inversely related to their length; that the lower the rank-order in frequency the more different words are found at that rank, and that the average number of different meanings for a word is proportionate to its frequency of occurrence.

If these findings are considered in relation to the lists of words in Tables I and II, one can see that of the 34 most frequently occurring only 7 are polysyllabic whereas of the 41 words having frequencies of less than five, 23 are polysyllabic. A consideration of these two tables also supports his second finding.

The number of different meanings per word has been calculated from the *Thorndike's English Dictionary* (1948). Zipf had used the *Thorndike Century Senior Dictionary* but this was unobtainable. In Figure 4 the number of meanings is plotted graphically against the rank-order of frequency. Zipf's proposition

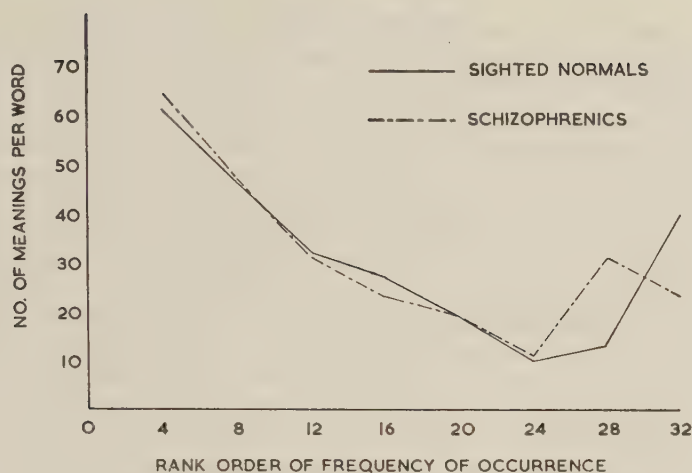


FIG. 4.

is confirmed for the first part of the curve but *face* and *back*, words of low frequency, have many meanings.

It seems quite clear that language behaviour plays a large part in determining the body concept obtained by the present method.

Schizophrenia and the Body Concept

In the symptomatology of schizophrenia there is often in Reitman's (1950) view a disturbance of the individual's concept of his own body and of the human body in general. This disorder of the body concept is depicted, he believes, in the schizophrenic's pictures of the body by "amputated limbs, mutilated bodies, detached heads, fusion of parts and the like."

Not all the studies of drawings of the human figure by schizophrenics have shown the changes noted by Reitman. Stonesifer (1949) using the Goodenough Scale found no significant differences between the drawings of male schizophrenics with an illness of less than 3 years' duration and normals. Smith (1953) found no difference in the time sequence of the parts drawn; while Chase (1941) found when scoring drawings by schizophrenics and normals on the Goodenough Scale that "scatter" of the items drawn was the prominent feature in the schizophrenic drawings.

Szasz (1957) and other authors with an interest in psycho-analysis believe that there is an increase in "libido tonus" either of the whole body or some organs, but offer no objective evidence. Presumably changes of this type would alter the body percept but if they do, there is no comparable change in the body concept. One wonders how much Reitman and other authors have been influenced by "special cases" where such changes do occur in the body concept.

Returning to a consideration of the word lists of body parts, it might be expected that schizophrenic disturbances in thinking, for example "over-inclusion", as described by Cameron (1944) or, the "loss of continuity in associations" (Bleuler, 1950), would be reflected in the lists.

While the list of irrelevant words in Table IV shows that there is "over-inclusion" by some schizophrenic subjects, the rank-order of frequency for the parts used by more than 25 per cent. of subjects is essentially the same as for normals (Tables I and III). In the 34 parts mentioned by more than 5 per cent.

of subjects only *ankle* is mentioned significantly less frequently than in normals. Sequences in associative listing which were calculated for normals and schizophrenics showed few differences and are not reported in detail.

From the point of view of language behaviour (Zipf, 1949), it is clear that as in normals the frequency of the occurrence of words is inversely related to their length and that the lower the rank-order in frequency, the more different words are found at that rank (Tables IV and V). The number of different meanings in relation to rank-order in frequency are plotted in Figure 4 as for normals, and it will be seen that the curve is almost identical.

In a further study of the relationship between the rank frequency distribution of words in schizophrenic language, Whitehorn and Zipf (1943) interpret their limited data in terms of opposing tendencies to "repetitiousness and diversification" in speech. The tendency to repetitiousness tends to increase frequency and diminishes the number of different words, whereas the tendency to diversification tends to increase the number of different words and diminish the relative frequency of their use. They equate the tendency to repetitiousness with autism. While their work is not entirely relevant to this study, since it involved the analysis of large quantities of written material, it does recognize that the correlation between word frequency and rank may, in schizophrenia, have other explanations than those suggested by Bousfield and Barclay (1950).

A Spearman rank-order correlation for the "schizophrenic" list of body parts of 0.38 was found between total frequency and mean rank order of mention. As stated previously, a figure of 0.57 was found in "normal sighted" lists. The correlation for schizophrenics is significantly less (at the 5 per cent. level) than that found for normal sighted subjects.

Apart from the tendency to a greater scatter in the results of the schizophrenics and the significantly lower correlation between frequency and rank-order of mention, the results are perhaps surprisingly similar to those obtained in normals. As far as the method of association listing goes, it does not seem to show a gross distortion of the body concept in chronic schizophrenic patients. It is hoped to present a study of the concepts of individual patients at a later date.

The Influence of Motivational Factors on the Body Concept

The present study was not designed to investigate the influence of motivational factors on the body concept but certain observations are relevant. Nothing can be said of the effects of intelligence although these have been studied extensively by Goodenough (1926). Sex appears to have less effect than might have been expected from the work of other authors. The small differences noted are of doubtful significance. In Goodenough's study sex differences depend more on clothing characteristics and differences in the proportions of various parts than on their presence or absence. Such differences in the male and female concepts would not, therefore, be demonstrated in the present investigation. The influence of other motivational factors is even more obscure and the present study does little to clarify the problem although the associative listing method of investigating the body concept might be a useful research tool in the investigation of the claims of such workers as Machover (1949). Machover believes that in the "draw a person" test the individual draws consciously or unconsciously on the whole system of psychic values and she attempts to assess personality structure from the drawings obtained. Her work has been examined critically by Copeland (1952), who points out the lack of

statistical data, the arbitrary nature of the interpretations and the theoretical confusions, particularly in relation to the Body Image concept, and concludes, as we must do, that much work remains to be done before the study of body concept can lead to a study of personality and motivation. Swensen (1957) has reviewed research on the "draw a person" test over the past eight years and concludes that Machover's hypotheses have seldom been supported. Motivational factors certainly operate as censors and there is only one mention of sexual parts in our investigation, while the erogenic zones stressed by Schilder do not receive particular mention.

Two other motivational factors must be mentioned. The first is the subject's attitude to the word "body". Foley and MacMillan (1943) investigated the associations of law, medical and non-professional students to 40 stimulus words. They found professional groups gave "professional interpretations" significantly more often. For this reason we excluded doctors and nurses from the "sighted normal" group. The second factor is called by Osgood (1953) "the internal non-verbal context" by which he means the ways in which a man's moods, emotions and motives influenced his verbalization. Secord (1953) used a list of homonyms which had "bodily" and common "non-bodily" meanings in a word association test. He believed that subjects with the greater number of "bodily" associations were those most concerned about their bodies.

The Body Schema and the Body Concept

The body schema as defined by Head and Holmes (1911) is a purely physiological mechanism operating outside consciousness and related to the sensory cortex. It is to this body schema, rather than to the body percept, that Wright (1956) has attempted to relate word frequency lists of body parts when he compares them with the areas of sensorimotor cortical representation as determined by the experiments of Penfield and Rasmussen (1950). He concluded that there was a strong possibility that the linguistic importance of the name of a part of the body was a function of the sensorimotor importance of that part. It is impossible to argue the matter in detail, but his views are not supported by our findings and two points which seem to contradict his views will be mentioned. It is impossible to explain the differences which occur between the sighted and totally blind subjects, for example the occurrence of the *nose* and *eye* as two of the parts first mentioned by the blind, when they are much less frequently mentioned by the sighted subjects. All the other differences which occur between the totally blind and sighted subjects argue against a relationship between linguistic frequency and sensorimotor representation. Wright found too, a remarkable correspondence between the ratio of the number of columns devoted to the upper and lower limbs in the *Oxford English Dictionary* (O.E.D.) and the ratio of the respective areas of cortical representation as determined by Penfield and Rasmussen. Wright's "linguistic" (O.E.D. columns) ratio upper limb/lower limb was 1.49/1 and the "neurological" (sensorimotor cortical representation) ratio was also 1.49/1. In the present study 6 upper limb parts are mentioned compared with 7 lower limb parts and if their frequencies are totalled this gives an upper limb/lower limb ratio of 317/350 or 0.9/1 which does not compare as favourably with the "neurological" ratio of 1.49/1. There may well be a relationship between body schema and body concept, but it seems that to attempt to relate a body concept obtained solely from Semantic Frequency lists with the areas of sensorimotor cortical representation overlooks some of the complexities of the body concept.

Bender, Green and Fink (1954) applying simultaneous tactile stimulation involving different body combinations to patients with organic mental syndrome, normal children, normal adults and schizophrenic adults, demonstrated a pattern in cutaneous perception not previously recognized. In this pattern the face as well as the genital region was the most perceptive and dominant body area, whereas the hand showed the least dominance. The remainder of the body regions fell between these two extremes in the form of a mild gradient. Bender and his colleagues attempted without success to explain this pattern which has no relationship to the body schema. It is clear from the present findings that it has no reference to the body concept as determined by this test.

Cohn (1953) proposed on the basis of similar findings from simultaneous tactile stimulation the principle of rostral dominance. By this he meant that the face was the most dominant part while the remaining body areas showed a descending gradient along the longitudinal axis of the body. He thought that for children under 5 years the patterns of their drawings of a boy and girl supported this view. As can be seen there is no evidence of any rostral dominance principle in our word tests.

SUMMARY

1. An attempt is made to define the term "body concept" and to describe one such concept elicited by a method of associative listing.

2. The differences between the concepts obtained from sighted individuals, those totally blind from birth and schizophrenics are described and analysed.

3. Relationships between the body concept and the schematic stage of children's drawings of the human figure are discussed.

4. The influence on the concept of primary and secondary perception together with other factors is discussed with special reference to visual perception and "facial vision" in the blind.

5. The effect of language behaviour on a body concept obtained by the method of associative listing is demonstrated.

6. Similarities and differences between the body concept of schizophrenics and normals are emphasized and the effect of motivation considered.

7. Reference is made to the lack of a clearly demonstrable relationship between the body schema and the body concept.

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RESPONSE TO SOME STIMULANT AND DEPRESSANT DRUGS OF THE CENTRAL NERVOUS SYSTEM

By

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NEARLY one hundred years ago, Anstie (1864) wrote: "Among the too frequent instances which are to be found in medical nomenclature, of confusion and uncertainty in the application of descriptive terms, there is none, perhaps, more striking than is occupied by the words Narcotic and Stimulant." Both classes of substance embrace drugs of antiquity. Thus of the depressants, alcohol dates from the time of the Thracian god, Dionysus, while the earliest use of stimulants such as caffeine and xanthine is lost in the obscurity of the past (Goodman and Gilman, 1955a). Even today, there exists no systematized codification of response to the two classes of drug, although it is implicitly assumed that stimulants and depressants are invariably and mutually antagonistic in their effect on the central nervous system. Advantage was therefore taken of phenomena arising during drug intoxications to categorize abnormal features in the central nervous system common to each of the two classes of intoxicant and to essay a comparison, the one with the other.

CASE MATERIAL

The material presented is a representative proportion of a considerably larger number of intoxications seen, aspects of which have already been reported (Marley, 1955; Marley and Chambers, 1956). Before conceding a diagnosis of drug intoxication, there are certain criteria to be satisfied. It must be certain (1) that the symptoms (or signs) arise *de novo* following drug ingestion and are not merely grafted on to an antedating illness; (2) the symptoms (or signs) are not due to drug withdrawal; (3) the clinical picture is temporary and reversible, the physical signs disappearing in 1-2 weeks, and the anomalies in the mental state abating ideally within 1 month and at most 2 months, and (4) if possible the diagnosis should be confirmed by blood or urine tests for the intoxicant (e.g. bromides, barbiturates, methylpentynol or its carbamate, and the amphetamine group). It is difficult to abide by all these strictures. Considering each of the desiderata in turn: (1) individuals with affective swings may take to drugs during a depressive phase, and it can then be hard to ascertain which symptoms are due to the intoxicant and which to the underlying illness (Cases 5, 10, 17 are examples); (2) while withdrawal symptoms are elusive with stimulant drugs, definite withdrawal symptoms occurred in only one of the depressant group (Case 4) on the fourth day of reduction of drug dose in hospital. Features ascribed to a drug must therefore be present before reduction of dosage, let alone withdrawal; (3) one to two months may seem excessive

for allowing the disappearance of abnormalities in the mental state. However, Connell (1958a) has emphasized the futility of attaching importance to the continuation of symptoms in amphetamine psychosis unless it is certain that the patient has no access to the drug. This qualification holds for intoxication with other drugs. As amphetamine psychosis may be indistinguishable from schizophrenia (Connell, 1958b) the importance of a follow-up period is obvious. Consideration must also be given to the possibility that amphetamine intoxication may rekindle "quiescent" schizophrenia, or that a brief reversible intoxication resembling schizophrenia may occur in a person previously diagnosed as schizophrenic, and (4) the picture of intoxication may be due to a combination of drugs, one or other predominating. These controversial facets have been given due weight in the selection of the material, the consistent ideal being to include only intoxications with unequivocal diagnoses.

Those intoxications presented are due to inorganic salts (bromides), aliphatic substances such as alcohols (paraldehyde and methylpentynol), substituted alcohols (chloral hydrate), esters (meprobamate, methylpentynol carbamate), aromatic substances such as the salts of barbituric acid (amyl-barbitone sodium, phenobarbitone) and the phenyl-alkylamines (amphetamine sulphate, dextro- and methyl-substituted amphetamines, and Preludin). Of the 27 subjects studied, 18 were seen and followed up personally by the author (Cases 1, 4, 6, 7, 10-16, 19, 21, 23-27). To modulate possible observer bias, details of a further nine were taken from the Maudsley Hospital notes. Cases 1-16 are those due to intoxication with central nervous system depressants, and Cases 17-27 subjects suffering from intoxication with central stimulants. (The term central stimulant is used throughout this paper specifically to connote the psychomotor stimulants belonging to the phenyl-alkylamine series and does not include other analeptic or convulsant drugs. Apart from the amphetamines and Preludin, the phenyl-alkyl amines in current use include ephedrine, Meratran, and Ritalin). Details relating to the particular intoxicant are given in Table I. Thus Cases 1 and 2 are paraldehyde intoxications, subjects 3-5 suffered from chloral hydrate poisoning and subjects 6 and 7 from bromism, subjects 8-11 were barbiturate intoxications, subjects 12-15 were cases of intoxication with methylpentynol or its carbamate (Oblivon or Oblivon C) and subject 16 is an instance of meprobamate poisoning (Miltown, 2-methyl-2-n-propyl-1, 3-propanediol dicarbamate). Of the stimulant intoxications, Cases 17-23 and 27 were due to one or other of the amphetamines, while Cases 24-26 were ascribed to Preludin (2-phenyl-3-methyl tetrahydro-1, 4-oxazine hydrochloride). Evidence incriminating the suspected intoxicant often came from finding it in the patient's belongings (Cases 2, 4, 7, 9, 11-13, 16, 18, 19, 23, 24, 26). The majority of the patients suffered from acute or chronic intoxications (Cases 1-9, 17-21, 27) the rest being acute intoxications. The dose of drug and its period of ingestion is that admitted by the patient and must in most instances be regarded as suspect. A large number of the subjects, particularly those with stimulant intoxications had abused other drugs in the past. Fourteen of the subjects were psychopathic personalities (Cases 2, 3, 6, 7, 9, 14, 16, 18-20, 22, 24-27) while six suffered from mood swings or a more serious affective illness (Cases 5, 10, 11, 17, 21, 23). Of the rest, five suffered from neurotic illnesses (Cases 1, 4, 8, 12, 15) and one (Case 13) from paranoid schizophrenia. The age and sex of the patient, together with positive results of tests for intoxicants are also shown in Table I. Unless stipulated, the serum bromide value for all patients was less than 25 mg./100 ml., and the W.R. and Kahn reactions negative. Details of the lapse of time for recovery both of the

TABLE I
Data Relating to 27 Patients with Various Drug Intoxications

Case No.	Age (years)	Sex	Drug	Admitted Duration (days)	Admitted Dose/Day	Diagnosis	Special Investigations	Other Drugs Previously Abused
1	42	M	Paraldehyde	3 months	12 drachms or more	"Anxiety hysteria"		Barbiturates.
2	37	F	Paraldehyde	1 year	18-24 drachms	Psychopathic personality		? none.
3	43	M	Chloral hydrate	?	?	Psychopathic personality		Alcohol, barbiturates, Carbromal.
4	37	M	Chloral hydrate	3 months	Up to 250 gr.	Neurotic depressive reaction		Alcohol, Sodium Amytal, paraldehyde.
5	55	F	Chloral hydrate	18 months	30 gr.	? Involuntional depression		None.
6	41	F	"Mist Three Fifteens" (Potassium bromide 15 gr., Chloral hydrate 15 gr., Tinct. opii. 15 minims)	10 years	2-12 x stipulated dose	"Inadequate personality"	Serum bromide 300 mg./ml. on admission	Drimamyl.
7	52	F	Mist pot. brom. (10 gr.) and chloral (5 gr.)	3 months	6-10 x stipulated dose	Psychopathic personality	Serum bromide 250 mg./ml. on admission	Alcohol, chloral hydrate paraldehyde.
8	50	M	Sodium Amytal	8 years	18-20 gr.	Anxiety state		None.
9	24	F	Sodium Amytal	15 months	12-36 gr. ?	Psychopathic personality	Serum barbiturates 2.1 mg./100 ml.	Other barbiturates.
10	43	F	Sodium Amytal	16 days		Manic-depressive psychosis		None.
11	29	F	Phenobarbitone	2 days	10 gr.	Neurotic depressive reaction		Obivon.
12	27	F	Methylpentynol	7-14 days	1-2 g.	Hysteria		Barbiturates.
13	46	M	Methylpentynol	2 days	5.0 g.	Paranoid schizophrenia	Whole blood methylpentynol 0.05 mg./ml.	None.
14	36	F	Methylpentynol	4 days	1.5 g.	Psychopathic personality		Alcohol
15	45	F	Methylpentynol carbamate	5 days	2.0 g.	Neurotic depressive reaction		None.
16	28	F	Meprobamate	3 days	2.8 g.	Psychopathic personality		? none.
17	40	M	M-amphetamine	1 year	?	Recurrent depression	Amphetamine-like substances in urine 1.5 mg./100 ml.	Alcohol, barbiturates, Carbromal, Obivon.
18	39	M	Amphetamine	2 months	Up to 65 mg. (salt)	Psychopathic personality	Amphetamine-like substances in urine 0.28 mg./100 ml.	Amytal, m-amphetamine.
19	55	M	D-amphetamine	8 months	10-30 mg. (salt)	Psychopathic personality	Amphetamine-like substances in urine 0.28 mg./100 ml.	? none.
20	25	F	D-amphetamine	2 years	Recently 100-150 mg. (salt)	Psychopathic personality	Amphetamine-like substances in urine > 1.5 mg./100 ml.	Barbiturates, codeine, morphine.
21	48	M	D-amphetamine	3 months	25 mg. (salt)	Manic-depressive psychosis	Amphetamine-like substances in urine > 1.5 mg./100 ml.	Alcohol.
22	35	M	Amphetamine	3 months	25-75 mg. Recently 250 mg. (salt)	Psychopathic personality	Amphetamine-like substances in urine > 1.5 mg./100 ml.	Barbiturates, morphine, pethidine.
23	28	M	Nasotrone by inhalation	3 days	325 mg. base in last 3 days	Recurrent depression	Amphetamine-like substances in urine > 1.2 mg./100 ml.	Amphetamine, Preludin.
24	34	F	Preludin	7 days	0.5 mg. (salt)	Psychopathic personality		Amphetamine, d-amphetamine.
25	32	F	Preludin	9 months	0.25 mg. (salt)	Psychopathic personality		? none.
26	31	F	Preludin	6 months	0.5 mg. (salt)	Psychopathic personality		D-amphetamine, alcohol.
27	44	M	Amphetamine	10 years	Recently 500 mg. (salt)	Psychopathic personality		Alcohol, barbiturates, chloral hydrate.

physical signs and the mental state is depicted in Table II. Uncertainty as to the time of disappearance of the physical signs exists for three patients (Cases 3, 17, 20) and in two for recovery of the mental state (Cases 3, 20). For the rest, all physical signs had gone within 2 weeks of drug withdrawal, resolution of

TABLE II
Duration of Abnormal Signs and Symptoms Following Drug Withdrawal

Case No.	Physical Signs	Mental State
1	4 days	Incomplete recovery by 7 months
2	2 weeks	2 weeks
3		Not Known
4	<7 days	<7 days
5	2 weeks	3 months
6	10 days	10 days
7	2 weeks	1 week
8	1 week	1 month
9	<6 days	<6 days
10	6 days	Incomplete recovery by 2 months
11	3 days	1 month
12	4 days	4 days
13	1 week	1 week
14	4 days	10 days
15	3 days	3 days
16	3 days	1 week
17	Not known	Incomplete recovery by 5 months
18	<7 days	<7 days
19	5 days	8 days
20		Not Known
21	<7 days	3 weeks
22	2 weeks	2 weeks
23	<7 days	1 week
24	1 week	1 week
25	3 days	1 week
26	1 week	2 weeks
27	10 days	10 days

the mental anomalies occurring within the prescribed 2 month period except for Cases 5, 17. The physical and mental abnormalities associated with the intoxications are now considered.

Physical Signs. The physical anomalies referable to the central nervous system are depicted in Figure 1a. For the depressant drugs there is an emphasis

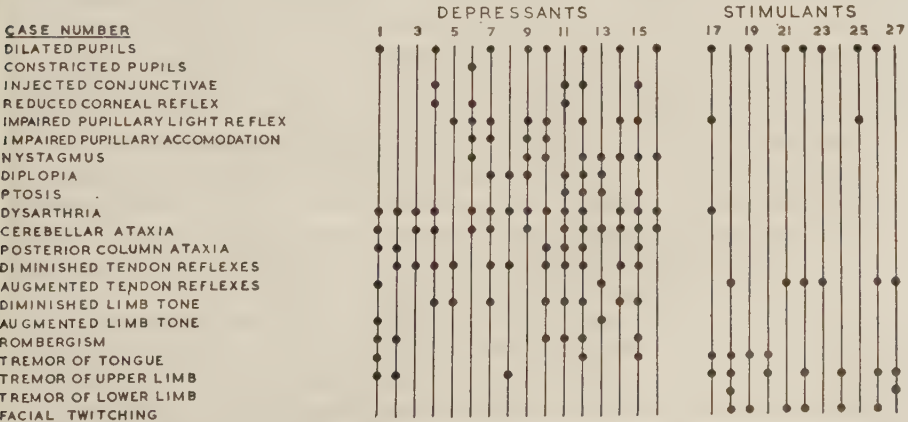


FIG. 1a.—Abnormal physical signs referable to the central nervous system found in 27 persons suffering from drug intoxications.

upon ataxic phenomena, cerebellar ataxia being found in 12 patients (Cases 1, 3, 4, 6, 7, 9, 11–16) and posterior column ataxia in six (Cases 1, 2, 10–12, 15). Typical of the specific cerebellar features were those seen in Case 12 in whom rapidly alternating movements were made clumsily, and on the finger-nose and heel-shin tests there was ataxia not compensated for by vision. Ataxic accompaniments included sustained horizontal nystagmus on conjugate lateral deviation of the eyes (Cases 6, 9, 10, 12–16), dysarthria (Cases 1–4, 6–12, 14–16) and Rombergism (Cases 1, 2, 9–11, 15). Other phenomena implying loss of muscle tone were ptosis, which might be accompanied by over-action of the frontalis muscle (Cases 11–13, 15), reduced corneal reflexes which were considered significant only if there was loss of facial muscle tone (Cases 4, 6, 11) and reduced tendon reflexes (Cases 2–5, 7, 8, 10–12, 14, 15). Increased limb tone, together with augmented tendon reflexes might be found in association with ataxic phenomena (Cases 1, 13). Thus the picture in Case 13 comprised rhythmic nystagmus on conjugate lateral deviation of the eyes, with diplopia in all directions of gaze, and right-sided ptosis. The gait was ataxic with a negative Romberg sign. Muscular tone was increased with positive Hoffman and Wartenberg signs and augmented tendon reflexes.

Equal bilateral dilatation of the pupils was noted in eight instances (Cases 1, 4, 7, 9, 10, 12, 14, 16) with sluggish direct and consensual responses to light (Cases 5–7, 9, 10, 12, 14, 15) and an impaired accommodation-convergence reflex (Cases 6, 7, 9, 10). In spite of the absence of paralytic strabismus or of any apparent disturbance of reflex conjugate lateral or vertical gaze, erroneous projection of the visual field was noted in six patients (Cases 7–9, 11–13).

The anomalies encountered with the central stimulants were of a different order. Thus, although equal bilateral dilatation of the pupils of 8–10 mm. diameter were found in 7 of the 10 subjects, an impaired direct or consensual response to light was found in only two (Cases 17, 25) while there was no alteration of the accommodation-convergence response. Perhaps the most striking difference from the depressant intoxications was the absence of ataxic features. Instead, there was increase of limb tone and augmented tendon reflexes (Cases 18, 21–23, 26) together with tremor of the tongue and/or upper limb (Cases 17, 18, 20, 22, 24, 26). Facial twitching (Cases 18, 19, 21, 22, 24, 26) was also noted. This seemed part myoclonic, i.e. brief shock-like contractions confined to the facial muscles, and part tic, i.e. repetitive movements involving the face and upper limb, particularly “hand-face” touching and plucking.

Many intoxications occur in subjects taking large quantities of either a medley of depressant and stimulant drugs (e.g. alcohol, barbiturates and amphetamine) or of a compound substance such as Drinamyl (amylorbarbitone and d-amphetamine). The signs usually present are those of the depressant drug intoxications. To quote two examples (not shown in Fig. 1a), the first (an individual taking amphetamine, barbiturates, methylpentynol) exhibited tremor of the out-stretched tongue and upper limb, and was dysarthric and ataxic: the other (ingesting Drinamyl), had nystagmus, dysarthria, and cerebellar ataxia with diminished tendon jerks.

Mental State. A synoptic version of the abnormalities in the mental state are shown in Figure 1b. The predominating behavioural anomalies were drowsiness with the depressant drugs (Cases 1, 4, 6, 7, 10–16) and excessive activity both at rest or in motion with the stimulants (Cases 17–19, 22–24, 26, 27). Typical descriptions for the depressants are (Case 12) “Drowsy on admission. The patient spent the first day asleep in bed, but is restless and wakeful at night.



FIG. 1b.—Alterations in the mental state for 27 persons suffering from drug intoxications.

She may be talking to you one moment and then suddenly falls asleep", or in an extreme instance (Case 6) "stuporose on admission with slight response to painful stimuli. A few hours later, there were movements and muffled answers to questions. The speech was slurred". Typical for the stimulant drugs is subject 22. He was "fidgety, moving and changing his position frequently. He played with his hand on the table or passed his hand over his face, rubbing his eyes and pulling at his spectacles".

Mood changes with the depressants were mostly depression combined with irritability. The depressive component may be quite marked. Thus one subject stated (Case 8), "I just feel depressed—that life is not worth living. I have thought of committing suicide by an overdose of drugs. No treatment has done me any good. I have no interest in anything." Another patient (Case 9) remarked "I wish I was dead. I've had enough of it. I can't stand it any longer. Oh, my head. What is wrong with it? Am I insane? Oh my children, my children" (weeps). There was a broader spectrum of mood change with the stimulants although depressive features might be found (Cases 17, 20, 22, 25) reaching even psychotic dimensions (Case 25). Fear was conspicuous in three subjects (Cases 22, 24, 26); rather surprisingly elation was found in only one stimulant intoxication (Case 23).

Thought, and its consort conversation, are particularly swayed by the affective state. As noted above there were ideas of suicide in those individuals who became depressed. Thus four subjects intoxicated with depressant drugs

(Cases 5, 8, 14, 16) and two with the stimulants (Cases 17, 26) expressed suicidal ideas. Ideas of unworthiness were found in three depressant intoxications (Cases 9, 11, 12) and one of the stimulants (Case 25). Slowness of thinking was marked in patients who were drowsy. In contrast, subjects with stimulant intoxications were often over-talkative, evincing ideas of reference (Cases 17-24, 26) and paranoid material (Cases 17, 20-24, 26). Thus (Case 26) the patient believed that her man friend was outside the house waiting with a gun to shoot her. She became frightened to go out and even afraid of the people in the house. "She would hear footsteps and then see the doorhandle turn. Someone was going to shoot her. There were women's voices calling her a prostitute". Another (Case 21) believed he was wanted by M.I.5. "They were getting at him through the telephone system". Ideas of reference, although present, were less common with the depressant intoxications (Cases 1, 3, 7, 11, 16). One patient (Case 7) "heard people on the ward planning to go and raid her house. They were going to steal her pictures and books. The nurses were communists and this was part of a communist plot." Ideas of influence were also found with the stimulants (Cases 22, 23). Only one subject was grandiose (Case 23). He insisted that he was brother of the Queen. This patient also showed disconnection of thought. The following is an abstract from one of his letters. "Made me altar hand. Righting boat and encore. Remember seing insect. Could it be a baby elefant, but had never seen an elefant. Word ending in G Rug, Bug, Tug." Dysphasic and paraphasic disorders were found only with the depressants, but although not elicited it would be unrealistic to suppose that they do not occur with stimulant intoxications.

Illusions were noted in four instances (Cases 1, 6, 20, 22). One (Case 1) thought that there was a man crouching down where actually there was just a chair. Visual and auditory hallucinations occurred in both groups (Cases 1, 6, 7, 12, 14, 18, 22, 24-26) there being a predominance of auditory hallucinations with the stimulants. Whereas those found with the stimulant intoxications occurred both during the day and night, there was a definite nocturnal emphasis for those with the depressant intoxications. Even if the patient had previously experienced auditory hallucinations under the influence of the drug, on subsequent occurrence they still bore the stamp of authenticity. One subject commented (Case 22) that "before taking the drug (amphetamine) he says to himself that he is going to hear the voices". Yet when they occur, "they are absolutely real". Visual hallucinations were complex rather than simple.

Disorientation for time was noted in six of the depressant group (Cases 4-7, 14, 15) and disorientation for all modalities in one (Case 6). Temporal disorientation was elicited in three of the stimulant intoxications (Cases 18, 21, 24).

Depersonalization and/or derealization were found in two subjects (Cases 5, 20). This probably underestimates the true incidence, their presence escaping the patient possibly because of impaired attention, concentration, or recent memory. The antithesis may also occur. One subject (Case 27) remarked, "Things are more real. Everything looks more alive and coloured." Another subject commented (Case 22) that after the drug "sounds outside the room appear magnified and louder. They are related to me". Body-image disturbances were also complained of. One of the more interesting was that of Case 22. He stated that within 10-15 minutes of ingesting a large quantity of drug, "his whole body would feel swollen". This was associated with a sensation of flushing.

Impaired attention and concentration were elicited regularly in both

groups of intoxications (Cases 1, 5-7, 9, 11-15, 17-20, 24, 26, 27) as was impairment of memory for recent events (Cases 1, 5, 6, 9, 11, 12, 14, 18, 22). Diminished insight was much more common with the stimulant intoxications. One patient (Case 19) ascribed his admission to hospital to "My whole trouble started by being 10 minutes late. There was nobody at the reception office and I was there until quarter-to-twelve."

DISCUSSION

The material presented above was selected because of the presence of physical signs referable to the central nervous system together with abnormal mental phenomena. It is not intended to suggest that they are the exclusive prototype of all intoxications with central stimulants or depressants, for these may manifest with none, or a minima of signs and symptoms.

It is hoped that the divergent character of the spectra of signs produced by central depressants or stimulants is apparent. It seems that abnormal signs are more likely to follow intoxication with the depressant drugs. Washburne (1934) describes double vision, sluggish pupillary reactions, ataxia of gait and speech, tremors and abolition or diminution of corneal, abdominal, knee and ankle reflexes in association with bromism, Isbell (1950) noted ataxia of gait and station, dysarthria, dysnergia, adiadochokinesis, hypotonia, tremor, depressed abdominal reflexes, and occasionally transient clonus and Babinski signs with chronic barbiturate intoxications. Nystagmus also occurs, being reproducible by the intravenous injection of quick-acting barbiturates (Bender and Brown, 1948). Bender and O'Brien (1946) attribute barbiturate nystagmus to the drug interfering both with control of eye movements and ocular fixation, an effect demonstrable in animals (Spiegel and Collins, 1940). Nystagmus was never found with intoxication by central stimulants, and contrasts with the fact that optokinetic nystagmus or that induced by labyrinthine stimulation is elicited with greater difficulty after central depressants but facilitated by central stimulants (Cogan, 1948). Curran (1938) feels that nystagmus is infrequent in bromism, but Copas *et al.* (1959) refer to it with "carbromal poisoning". Alcohol intoxication may present with mydriasis, impaired pupillary responses, suffused conjunctivae, nystagmus, and ataxia with a positive Romberg sign (Howells, 1952). Drowsiness is one of the principal side-effects of meprobamate (Hinton, 1958) although coma and neurological signs have been encountered (Heberden and Cooper, 1957; Bedson, 1959). With methylpentynol intoxications the abnormalities include pupillary reflex anomalies, nystagmus, dysarthria, tremor of the protruded tongue, and cerebellar ataxy in the limbs or admixtures of this with posterior column ataxia. Muscular tone was usually diminished as were the tendon reflexes (Marley and Chambers, 1958). Similar signs were found with methylpentynol carbamate intoxications (Bartholomew *et al.*, 1958; Marley, 1958). Hypotonia with normal or exaggerated tendon reflexes was occasionally seen with the depressant intoxications. Kremer (1958) discusses this anachronism in the light of work by Hammond *et al.*, (1958) on the function of the α and γ efferent nerve fibres to the muscle and muscle spindles. That the effect of paraldehyde, chloral hydrate and the barbiturates in reducing muscle tone is a central action and not on the muscle itself or the neuromuscular junction was confirmed by Quilliam (1955) the same being true for methylpentynol and its carbamate (Marley, 1959a).

The nervous system signs with stimulant intoxications are less dramatic. Connell (1958c) feels that there are no specific signs of amphetamine intoxication,

and indeed alludes to the few references to the physical state in amphetamine poisoning (Connell, 1958d). In the cases mentioned here, a coterie of signs, not all invariably present, stand out. These are mydriasis with occasionally impaired pupillary response to light and accommodation, tremor of the tongue and limbs, augmented tendon jerks with increased limb tone, and facial tics and twitching.

Dilatation of the pupils or "spastic mydriasis" occurs with either central depressants (Duke-Elder, 1949a) or stimulants (Duke-Elder, 1949b). There may be diminished or absent reflex pupillary changes to light and convergence, although an "incomplete light rigidity" (Duke-Elder, 1949c) is more likely, the pupillary reflex to light being impaired before that to convergence (Duke-Elder, 1949d). The phenyl-alkylamines have been used as mydriatics (Myerson and Thau, 1938; Mayer, 1939) and Goodman and Gilman (1955b) comment that the light reflex is not affected except after repeated local instillation of amphetamine into the conjunctival sac, an effect which is rarely seen after its systemic administration in man. Nevertheless, mydriasis with amphetamine (or other phenyl-alkylamine) intoxications have been reported in man (Shorvon, 1945; Herman and Nagler, 1954; Martimor *et al.*, 1955; Patuck, 1956; Shanson, 1956) and in animals (Stern, 1889; Dale and Laidlaw, 1912; Udenfriend *et al.*, 1957). Of Connell's 42 cases, 12 had dilated pupils and 3 an impaired light response (Connell, 1958c).

The association of mydriasis with or without an impaired light reaction was found with both amphetamine and Preludin intoxications. In an attempt to elucidate the mechanism of this effect, cats were given various phenyl-alkylamines intravenously. Considerably greater doses were required to produce impairment of reflex response to light than for mydriasis. The pupillary dilatation could be elicited after immediate removal of both superior cervical ganglia, both suprarenal glands and unilateral resection of the ciliary ganglion. If the post-ganglionic cervical sympathetic trunk was allowed to degenerate after removal of the superior cervical ganglion, then homolateral pupillary dilatation was either absent or minimal with these drugs (Marley, 1959, unpublished data). The production of mydriasis with amphetamine or Preludin must therefore depend partly on the integrity of post-ganglionic sympathetic nerve endings in the iris.

Mydriasis, tremor, and restlessness occur after overdoses of ephedrine (Goodman and Gilman, 1955c) and the drug may produce a picture not at all unlike amphetamine intoxication (Locket, 1957a). Tremor in humans after amphetamine was mentioned by Monroe and Drell (1947) and Knapp (1952) and may occur in animals after central stimulants (Alles, 1927; Chen and Bohner 1958). It is also seen in poisoning with the caffeine-xanthine group of stimulants (Locket, 1957b). Deniker (1957) describes mydriasis and tremor after mescaline which is a central stimulant (Stockings, 1940; Speck, 1957). Tremor and augmented tendon jerks were noted with the amphetamine and Preludin intoxications and one may speculate whether it is due to the drugs increasing the servo instability in the stretch reflex arc, a mechanism proposed by Halliday and Redfearn (1956). Tremor of the tongue and upper limb may be found with the central depressants, particularly the barbiturates (Maurer and Vogel, 1954), although it is more dramatic as a feature of drug withdrawal.

Facial twitching was also noted. Small tic-like movements of the hands, feet, eyes, ears, and especially of the lips and mouth with frequent touching of the naso-labial region have been produced in monkeys with amphetamine or Ritalin (Cole and Glees, 1957). Klüver (1958) describes an identical syn-

drome in these animals elicited by mescaline and other phenethylamine compounds. The facial twitching with the amphetamine and Preludin intoxications seemed part tic and part myoclonic in nature. The two interpretations are not irreconcilable, for Pfeiffer (1957) refers to photic-stimulation induced seizures in normal subjects receiving mescaline, and convulsions have followed an overdose of amphetamine (Apfelberg, 1938). In animals, fatal doses of amphetamine provoke tremors and clonic convulsions (Leake, 1958a).

Restlessness was also marked with the stimulant intoxications, and Fullerton (1956) found increased abnormal activity in humans after Meratran. Dews (1953) observed with mice that psychomotor stimulants such as cocaine or methamphetamine greatly increase co-ordinated activity, while central stimulants such as picrotoxin have no effect or depress activity. Central depressants usually decrease activity. Thus Laverty and Franks (1958) were impressed by the significant diminution of spontaneous movement following a non-hypnotic dose of barbiturate, and it can be shown quantitatively that pentobarbitone sodium or meprobamate significantly reduce movement during sleep (Hinton and Marley, 1959).

An explanation of the difference in response to the two classes of drugs may lie in their effect on the postural and righting reflexes. Analogies have mainly to be drawn from animal work, and impairment of postural mechanisms have been demonstrated to occur with alcohol (Versteegh, 1922; Alexandroff and Talpis, 1928) and with barbiturates (Hondelink, 1932; Beecher *et al.*, 1939). In contrast, righting and other postural activity returns in decerebrate cats after d-amphetamine (Maling and Acheson, 1946; Macht, 1950), after Meratran (Brown and Werner, 1954) and in decapitate dogs after ephedrine (Hinsey *et al.*, 1931). Factors such as these may account for the comparative absence of ataxic phenomena with stimulant intoxications and their abundance with the depressant drugs. Nevertheless, ataxy and cerebellar signs may occur in humans with amphetamine intoxication (Mathias, 1951) and cerebellar inco-ordination has been encountered with Preludin intoxications (Bartholomew and Marley, 1959). The presence of ataxic signs with stimulant drug intoxications could lead one to suspect the patient had also been taking depressant substances (alcohol, barbiturates, etc.). Certainly subjects given large doses of pentobarbitone sodium and leptazol have ataxy of gait and station, nystagmus and involuntary clonic jerks (Fazekas *et al.*, 1956) as they do after barbiturate and Bemigrade (Gershon and Shaw, 1957).

It would be only reasonable to expect a wide range of behavioural responses with these drugs. This was so, with an emphasis on drowsiness for the depressants and overactivity and restlessness with the stimulants. Restlessness and aggressive incidents may occur during depressant drug intoxications being possibly a catastrophic response to disorientation or impaired consciousness. Curran (1944) noted restlessness and hypomanic episodes with barbiturate poisoning, while Connell (1958f) in his superb monograph on amphetamine psychosis, mentions a plethora of behavioural anomalies, including "found wandering, suicidal attempt, violent behaviour, assaulting police" etc.

As behaviour and thought are affectively determined, the effect of drugs on mood is of cardinal importance. Depression with irritability was a salient feature of the depressant drug intoxications whereas there was a greater spectrum of mood pattern with the stimulant drugs, elation rather surprisingly being uncommon. Dissimilar effects on mood may be associated with the same drug. Thus of 54 patients prescribed methylpentynol, 14 became euphoric or elated and 23 depressed or irritable (Marley and Bartholomew, 1958). With both

depressants and stimulants, the mood response may initially be elation ultimately transforming to depression. It is for such reasons that affective changes following drug administration have been categorized as non-specific (Cleghorn, 1952). Elevation of mood is conventionally associated with the administration of amphetamine (Peoples and Guttman, 1936; Guttman and Sargant, 1937) and Preludin (Randell, 1957). However, depressive mood changes followed the ingestion of amphetamine or Preludin and this paradoxical affective response has not passed unheeded (O'Flanagan and Taylor, 1950; Leake, 1958b). Elation and depression may occur as complications of barbiturate therapy (Curran, 1944). In synopsis then "it would appear that the terms stimulant and depressant outside the isolated organ context are not specific enough to be rigidly adhered to. In the human frame of reference such drugs may produce antipodal mood effects even in the same person" (Marley, 1959b).

It was noted with methylpentynol intoxications that ideational content was congruous with the prevailing mood change (Marley and Bartholomew, 1958). Similarly, for the stimulant intoxications, appropriate thought content may be found with dissimilar affective changes. In this series, one patient on Preludin became severely depressed with typical depressive ideas and hallucinations. Ideas of reference occurred in both groups, but more so with the stimulants. Fully matured paranoid ideas were also commoner with the stimulant intoxications, although they may occur with the depressants and Isbell *et al.*, 1950 refer to patients with barbiturate intoxication who became euphoric or paranoid. The difference between thought content for the two groups of intoxications could be that with the depressants the drowsiness and difficulty in thinking vitiate the development of paranoid material, while with the stimulant intoxications the subject, if anything, registers a larger number of impressions, and this with perhaps misinterpretation of sensory cues due to impaired consciousness, commits him to delusional elaborations. Connell (1958g) describes the amphetamine psychosis (to whom its separate categorization is due) as a paranoid psychosis with ideas of reference and persecution, auditory and visual hallucinations, in a setting of clear consciousness. Paranoid reactions with the amphetamines were noted also by Freyhan (1949); Norman and Shea (1945); Knapp (1952); and Tolentino (1957); with cocaine intoxication (Bleuler, 1951) and with the phenyl-alkylamines Preludin (Bethell, 1957; Glatt, 1957) or Meratran (Begg and Reid, 1956). Transitory schizophrenic and paranoid states with clear consciousness may occur with depressant drugs (Levin, 1947).

Illusions and hallucinations are found with both central depressants (Curran, 1944) and with central stimulants such as the amphetamines (Wallis *et al.*, 1949; Carr, 1954). They tend to be mood determined and to relate to events in the patient's life. They might therefore be regarded as epi-phenomena. Noyes (1948a) remarks that not only are illusions likely to be determined by the prevailing trend of the patient's preoccupation, but that the mental material which is externalized in the form of hallucinations is of a most intimate, subjective and personal nature (Noyes, 1948b). In this series they were relatively commoner with the stimulants than the depressants, with a slight predominance (in the case of the stimulants) of the auditory over the visual. The phenomena occurred both during the day and at night with the stimulant intoxications, but were primarily nocturnal with the depressant drugs, a point emphasized by Wolff and Curran (1935).

Levin (1956) distinguishes between delirious and paranoid disorientation

and that found with organic brain disease. He considers the disorientation of toxic delirium the easiest to understand, being in Hughlings Jackson's words a "reduction to a more automatic condition" (Levin, 1936). Levin (1951) formulated the entity of "partial delirium", which depends on the fact that orientation for time, being an abstract concept, is more vulnerable and consequently more likely to be upset than orientation for place or person. This "partial delirium" was found in six of the depressant and three of the stimulant intoxications. Thus the majority of the patients were not delirious in the strict sense, and belong to what Cameron (1947) has termed the syndrome of progressive cerebral incompetence. A subacute delirious state with Preludin intoxication has in fact been reported (Silverman, 1959). Connell (1958g) noted the absence of disorientation as a symptom of amphetamine intoxication. Connell (1958h) also points out that the term toxic confusion is sometimes used to imply confusion with disorientation, at others to mean cognitive disturbance without disorientation. Impaired attention and concentration were found with ten of the depressant intoxications, and with six of the stimulants. That clouding of consciousness existed is evident from the incidence of impaired memory for recent events in both groups of intoxications. Impaired cognitive function with the depressant drugs is well known. Hoch (1906) and Kornetsky (1951) found declines in digit retention with either intoxications or prolonged drug administration. Weinstein and Kahn (1955) regard disorientation, re-duplication and paraphasia as manifestations of denial of illness rather than being specific deficits.

More piquant anomalies such as depersonalization, derealization and body-image disturbance did occur but were less frequent than might have been anticipated. Body-image disturbances were classifiable into Bonnier's (1905) category of *paraschematia*, the best examples of which are usually seen in drug intoxications (Critchley, 1950). The final striking feature with the stimulant drugs was the frequent loss of, or impairment of, insight during intoxication, an aspect nothing like so conspicuous with the depressant intoxications. This may be linked with the differing mental content with the two classes of drug response.

What generalizations emerge from this appraisal? Perhaps first the uniformity of response within each of the two groups of intoxicants. For the group of depressants, ataxic features dependent upon loss of muscle tone predominated, whereas enhancement of postural function seemed typical of the stimulant intoxications. The distinction between the mental anomalies produced by the two classes of intoxicant was not so forthright. Nevertheless, some categorization can be made, with an emphasis for the depressants on drowsiness, depression and irritability, slowness of thinking, impaired attention, concentration and memory for recent events. With the stimulants there was overactivity, garrulity, ideas of reference and paranoid features, impaired attention, concentration and memory for recent events, together with diminished insight. Allusion might also be made to the greater incidence of temporal disorientation with the depressants and auditory hallucinations with the stimulant intoxications. These distinguishing criteria are set out in Table III (p. 88).

The central depressant drugs considered here fall into the group of "hypno-sedatives and tranquillo-sedatives" designated by Jacobsen (1958). Other groups suggested by him are (1) the "major tranquillizers" (reserpine, chlorpromazine), (2) the "minor tranquillizers" (antihistamines) and (3) the "central acting anti-acetylcholines" (atropine, benactyzine). Ataxic phenomena may

TABLE III

Distinguishing Criteria between "Depressant" and "Stimulant" Drug Intoxications

	"Depressants"	"Stimulants"
Pupils	May be dilated; may be impaired reaction to light and accommodation.	May be dilated; may be impaired reaction to light and accommodation.
Nystagmus ..	Often present on conjugate deviation of the eyes.	Absent
Diplopia ..	May be present.	Absent
Ptosis	May be present.	Absent.
Facial twitching/tic	Facial twitching may be present during intoxication. Also a withdrawal sign.	Facial twitching often present during intoxication. "Hand-face" touching common.
Dysarthria ..	Often present.	Infrequently present.
Tremor	Exaggeration of physiological tremor, cerebellar or posterior column varieties. Marked during drug withdrawal.	Exaggeration of physiological tremor. Not a withdrawal sign.
Muscle tone ..	Usually decreased but can be augmented.	Usually augmented.
Tendon reflexes	Usually diminished.	Exaggerated.
Ataxia	Often present. Cerebellar or posterior column varieties.	Rare.
Spontaneous movements	Reduced in quantity and amplitude.	Frequent fidgeting. May be tics and grimacing.
Behaviour ..	Usually underactive, drowsy. May be excited. Restless at night.	Overactive, restless.
Mood	Any mood change. Usually, depressed and irritable.	Any mood change. Often anxiety, fear. Rarely elated.
Thought	Slow with poverty of thought. May be paranoid ideas.	May be disconnection of thought. Often paranoid ideas.
Illusions and hallucinations	Visual, predominantly nocturnal.	Auditory, and occur both day and night.
Orientation ..	Often temporal disorientation.	May be temporal disorientation.
Attention and concentration	Usually impaired.	Usually impaired.
Insight	Usually adequate.	Frequently impaired.
Withdrawal symptoms	May be marked.	Minimal.

occur with overdose of any of these groups but particularly (2) and (3) (White *et al.*, 1956; May, 1958; Baker and Farley, 1958), the righting reflexes usually being preserved even after large doses of (1) (Jacobsen, 1958). Other central depressants eluding the above classification include the analgesics morphine, pethidine, etc. Harris (1951a) envisaged a standard sequence of response to volatile or non-volatile anaesthetic drugs, implying thereby an orderly descending depression of central nervous function from the cerebrum via the midbrain to the medulla. Depressant drugs with an oil/water partition coefficient between unity and eight (amylobarbitone sodium, phenobarbitone, paraldehyde, methylpentynol and its carbamate) produce the standard sequence of response. In contrast, substances such as ethanol or chloral hydrate with an oil/water partition coefficient less than unity, depart from the sequence, the medulla being depressed coincidentally or soon after the cerebrum (Harris, 1951b). It is surprising then to encounter such uniformity of reaction to the cadre of depressant drugs, although this may devolve from some pharmaco-

logical action common to all. Apropos this, Nicholls and Quilliam (1956) suggested that paraldehyde and methylpentynol reduce the amount of acetylcholine (ACh) released at the neuromuscular junction, and it is known that the barbiturates (Exley, 1954) and methylpentynol as well as the carbamate (Marley and Paton, 1959) depress the release of ACh from the cat's superior cervical ganglion. This is not the simple answer to their mechanism for the morphine analogues also reduce the ACh output (Paton, 1957) but only infrequently produce ataxia in the human.

The central stimulants embrace not only convulsants such as picrotoxin, but also the psychomotor stimulants of which the phenyl-alkylamines have been taken here as the paradigm for study. Various pharmacological classifications of these substances have been proposed (Fleckenstein and Burn, 1953; Fleckenstein and Bass, 1955). Recently it has been suggested (Vane, 1958, personal communication) that the phenyl-alkylamines should be subdivided into (a) those mimicking (5HT) 5-hydroxytryptamine (amphetamine, mescaline, etc.), (b) those behaving like a mixture of 5HT and adrenaline (ephedrine, Preludin, etc.) and (c) those acting like adrenaline (dopamine, etc.). In this series, uniformity of response was found with drugs falling into the categories (a) and (b). The central action of amphetamine may be on receptors in the brain stem area (Bradley and Elkes, 1957) as has also been suggested for ephedrine, Meratran, and Ritalin (Himwich, 1959); certainly many of the side-effects with both the stimulant and depressant group of drugs indicate a brain stem locus of effect. Finally, while there is a great deal of overlap in response to the two groups of drugs, the dichotomy between them may be examples of what Davis (1950) considered failure of normal homeostasis, the one representing a too high level, the other a too low level at which regulation of the nervous system is being maintained.

SUMMARY

Twenty-seven instances of drug intoxication are presented, sixteen due to "central depressant substances" (bromides, paraldehyde, chloral hydrate, barbiturates, methylpentynol and its carbamate, meprobamate) and eleven due to "central stimulants" as specifically exemplified by the phenyl-alkylamines (amphetamine, d- and m- amphetamine, Preludin).

The nervous system physical signs found during intoxication with the "depressant" drugs consisted mainly of ataxic features (nystagmus, dysarthria, cerebellar and/or posterior column ataxia) and those dependent upon loss of muscle tone (ptosis, loss of limb tone and diminished tendon reflexes). In contrast, enhancement of postural function seemed typical of the "stimulant" intoxications, there being augmented limb tone and tendon reflexes. Other signs included mydriasis with impaired pupillary response to light, tremor of the tongue and limbs, and facial twitching and tics.

In the mental state, the emphasis with the "depressants" was on drowsiness, depression and irritability, slowness of thinking, impaired attention, concentration and memory for recent events. With the "stimulants" there was over-activity, garrulity, disconnection of thought, ideas of reference and paranoid features with diminished insight, impaired attention, concentration and memory for recent events. In addition, there was a greater incidence of temporal dis-orientation with the "depressant" drugs, and auditory hallucinations with the "stimulant" intoxications.

The internal uniformity of response (both for the physical signs and the

mental state) within each of the two cadres of intoxicants is discussed and, contrasted with the dissimilarity of response of the two groups as a whole, each to the other.

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ADDENDUM

Methods for estimating drugs in body fluids. The serum bromides were determined by the gold chloride method (Harrison, 1947), the serum barbiturates by the calorimetric method described by Varley (1954), methylpentynol by the technique of Marley and Vane (1958), and the amphetamines by the method of Connell (1958i).

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NATURAL HISTORY STUDIES IN MENTAL ILLNESS*

A DISCUSSION BASED ON A PILOT STUDY OF OBSESSIONAL STATES

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INTRODUCTION

THE history of mediaeval medicine shows clearly that the decline of a science takes place whenever the tendency to theorize overruns the desire to observe and measure. Psychiatry with its shorter medical history has suffered from this tendency until fairly recent times. Even now, it is possible to estimate the efficiency of a nation's psychiatric progress by comparing the amount of factual research with the emphasis placed on unproven theoretical concepts in clinical practice.

It may seem, however, that serious consideration of the natural history of mental illnesses, which have been recognized medically for a century or more, is superfluous. In fact, the importance of such studies has never been greater, for not only is there a need for a yardstick against which the effects of modern therapies may be measured, but there is the more pressing question of the toll taken of national efficiency by any given illness. Only by recognizing this can suitable steps be taken to assess the problem and to devote the necessary medical and other services to overcome it economically. Although many of the issues discussed are obvious, there is some justification for restating them in the light of changes which have taken place in psychiatry since early classical studies were undertaken. Despite the many investigations of isolated and grouped aspects of the course of mental illnesses, there is still a need for comprehensive research.

Certain changes are taking place which merit further consideration of this topic. First is the considerable interest now shown by public and Parliament in the problems of mental illness. It is also a fact that more effective therapies are available now than ever before. In addition, the medical profession and public are better informed, better able to detect early cases and more likely to bring such cases to the attention of the psychiatrist and research worker.

Previously, before more effective therapy was available, large studies were made which now form classics of psychiatric literature (Janet, 1903; Kraepelin, 1921); opportunities to study large samples of patients were not neglected, and the absence of treatment, as we now know it, readily provided a control group in which natural history could be measured. Unfortunately, only the simplest statistical tests were in use in psychiatry until fairly recently and, in addition, concepts of clinical entities were still being evolved so that even excellent clinical descriptions could not define many of the issues that are now significant.

* Awarded the Bronze Medal and Prize of the Royal Medico-Psychological Association for 1959.

Beside the inevitable inadequacy of measurement in early work, other factors were the gross severity of many of the illnesses studied, the samples being over-represented in this respect, and the tendency to group together clinical entities which are now separated, e.g. Janet (1903) included tics, "excitements", neurasthenia and depersonalization in his study of psychasthenia.

There is now a tendency in some quarters to regard longitudinal and casuistic studies unfavourably, but these methods have never been overworked, and they have been applied to comparatively few groups of illnesses. Lewis's remarks of over twenty years ago (1936) remain equally true today: "It would be a pity if other quests kept us from making sure of all the plain clinical things that are yet to be seen and studied." From the research worker's point of view such projects have the fortunate characteristic that they always produce a result.

In the present study, attention is first drawn to the subject as a whole. Later, the essentials of methodology applied to this topic are discussed and illustrated with reference to relevant published studies and original work carried out on a sample of obsessional neurotics.

INTERPRETATION AND SCOPE OF "NATURAL HISTORY"

Strictly speaking, natural history implies the study of natural phenomena relating to the earth, and to animal life particularly. The term also refers to that which is neither artificial nor pathological, but Ryle's (1936) use of the phrase in his work relating to somatic disease suggests its application to the field of mental disorders. It is not difficult to justify the use of such a descriptive concept, for it denotes far more than the mere course of the illness. The formal textbook method of describing psychiatric phenomena under aetiology, psychopathology, course, prognosis and treatment is an approach readily appreciated by the medical student, but the many variables altering and qualifying the statements made render it difficult, by this means alone, to see fully the problem set by an illness in an individual or the problem to psychiatry as a whole. A knowledge of natural history may be expected to bring better understanding of mental disorders which differ in so many respects from physical ailments.

Even those who deny that body and mind are one and indivisible would admit that the natural history of psychological illness is vastly more complex than that of somatic disorders. Many more factors influence the behaviour of man than influence the behaviour of his component parts, and the long-drawn-out catamnesis of most mental illnesses makes the study of their course more exacting and more lengthy. For this reason, the concept of natural history must be broad, and if the findings are to be useful, the notion should be such that it can be practically investigated. The following is suggested as a working definition: the natural history of a mental illness consists of the detailed development, course and decline of that illness in the lives of individuals in the mass, the characteristics of those individuals, the social effect of the illness, and the factors affecting the pathological processes.

There is no virtue in including under the phrase "natural history" all the facts known about an illness. Essentially, the total concept conveys as a unified whole the development, course and outcome of the illness, the community in which it developed and its incidence, even if this must be expressed statistically in terms of chance expectation.

The starting point is the incidence of the disorder in the general population,

and in psychiatric practice, and an estimate of sex incidence. The main milestones of the disease process, such as age of onset of first symptoms, periodicity of attacks, age at which incapacity occurs, age when first seeking medical or psychiatric advice, follow naturally and can be measured. More detailed study is required to ascertain the mode of onset, variation in severity of established symptoms, mode of recovery or decline, and personality. Particularly difficult is the assessment of prognosis, whether recovery is complete, whether impairment of function remains or whether the patient adjusts to the illness if it reaches a stationary condition. The factors related to prognosis can be statistically presented and aetiological factors investigated. From these data a life chart representing the behaviour of the illness, in an average sense, may be drawn.

With the laudable ubiquity of treatment at the present time there is no alternative to the study of patients whose illnesses have been modified in some way, but provided large samples are assessed and those treated by most effective therapies excluded, the results will still be of value for comparison with the effects of future treatments. For example, the reliable studies of the effect of leucotomy on the course of chronic severe obsessional neurosis (Partridge, 1950; Pippard, 1955) show that the operation produces improvement more often than any other therapy, and it would be reasonable to exclude leucotomized patients from a series used to study the natural outcome of the disorder. There would be little point in excluding patients treated by other methods since there is no firm evidence to suggest that these influence materially the long-term course. On the other hand, many modes of treatment such as reassurance, superficial psychotherapy, hypnosis, group therapy, sedatives and other physical therapies seem to be equally beneficial to sufferers from anxiety hysteria. The study of treated patients remains valuable because the results provide a measure of the virtue of current therapy which future methods should surpass.

At this stage, it may be thought that the adoption of a concept of natural history which includes the study of treated illness is likely to render the work fruitless and nullify the special use of a descriptive phrase. In the subsequent discussion, the alternatives are criticized with a view to encouraging the use of present-day clinical material. One possibility of avoiding patients who had received treatment would be the study of cases in general practice. This course might be suitable for the milder neurotic patient, but the series could never be representative of a disease entity, the interested practitioner would have difficulty in avoiding the administration of treatment in some form, and it would take many years to amass sufficient material from which to draw conclusions. Further, the results, although valuable to the general practitioner, would not apply to the vast majority of patients seen by psychiatrists, and the interpretations of findings from such a biased sample would be extremely difficult. Another method might consist in the investigation of patients whose illnesses occurred in the days when treatment was either ineffective or symptomatic. Unfortunately, the formal centres caring for patients thirty years ago admitted them under certificate only, and a sample drawn from such sources would over-represent severely ill individuals. In addition, less attention was paid to detailed records and differential diagnosis in the days before the existence of treatment made this far more important. A further criterion of selection of patients for investigation rests on the difficulty of separating what is pathological and what is personality, and it seems most practicable to choose patients who have been sufficiently ill to seek specialist medical advice or to have this sought for them.

In summary, the answer to these problems lies in rigid definition of the clinical entity selected, the acceptance of the fact that patients will have had some treatment—preferably conservative, and the study of large numbers of cases to include all degrees of severity of illness to allow for the operation of all the environmental and other factors likely to influence its course.

WHAT IS ALREADY KNOWN OF NATURAL HISTORY?

A brief review of the existing channels through which knowledge of the natural course of mental illness is gained may help to clarify some of the problems likely to be met in present-day research on this topic. Personal experience in clinical practice is probably the surest method of learning about the behaviour of any disease, but however diligent the physician, there is no short cut to the soundness of judgment possessed by those who have seen many cases over a long period. Arising from personal experience were the anecdotal reports—more in vogue formerly than now—showing the development of an individual's illness and his response to treatment. The general view nowadays would probably be that such reports are more valuable when they represent exceptions to, rather than examples of what has already been reported *en masse*. The misleading nature of some of the older reports need not be laboured, but there is still a tendency to accept findings in individual cases which appear superficially to confirm an hypothesis whilst the unsoundness of the principle that any number of isolated cases cannot prove the theory is ignored.

Official statistics of mental illness show many of the administrative problems, but being derived from multiple sources and being restricted to many statements which are ill-defined, the results are difficult to interpret in terms of clinical practice. However, casuistic examination of patients has provided valuable factual material, especially when large groups have been used. Very often circumstances may limit the scope of the work so that statistical methods cannot be used fully, but investigations of large samples, in detail and over a long period, form classics of psychiatric publication. Although many large-scale studies of patients with mental illnesses have appeared, they have rarely been comprehensive enough to include all the relevant factors, and subsequent attempts to combine the results of different studies in order to gain a complete picture are baulked by the operation of numerous variables in differing concentration in the various samples. Among these variables are definition of illness, length of follow-up, severity of illness and social grouping of the patients studied, and it is unfortunate that it is usually impossible to state categorically which variables are responsible for the differences between several series of results. As an illustration of this problem by the use of findings of eminent research workers, the figures of Kraepelin (1921) and of Slater (1938) regarding the age of onset of the first depressive attack in manic-depressive psychosis may be compared (Table I).

Although Kraepelin found two-thirds of patients in which the first attack began before the age of 40, Slater found two-thirds of patients commencing their illness after that age. Rennie (1942) found the greatest number of first attacks beginning between the ages of 45 and 55. The discrepancy between these results might readily be explained by assuming that Slater and Rennie included more cases of involutional depressive illness than Kraepelin, but this would amount to an assumption which these investigations were designed to prove or disprove.

TABLE I

Age of Onset of First Depressive Attack in Manic-Depressive Psychosis

Age Group (years)	Percentage of Patients Experiencing First Attack	
	Kraepelin	Slater
0-20	19.3	2
20-30	30.7	12
30-40	22.0	19
40-50	14.8	22
50-60	9.9	22
60-	3.3	23
	100%	100%

THE CONTRIBUTION OF NATURAL HISTORY

Quite apart from the philosophical value of knowing "the whole" when one can immediately experience but a part—a principle underlying orthodox psychiatric case-taking—knowledge of natural history may contribute to diagnosis, management and prognosis and provide a means of gauging the effect of therapy in addition to supplying facts of administrative significance.

Diagnosis in medicine usually derives from a train of processes as follows: (a) fact gathering—the full case history and physical examination; (b) fitting the facts into a pattern; (c) comparing the pattern with what is known of the phenomena and natural history of diseases; (d) deciding which known entity the pattern most closely resembles. As emphasis in this article is on the numerical appraisal of massed data as opposed to the anecdotal method, case histories have been omitted. The following four examples are used to try to illustrate some ways in which the facts of natural history might be used, to show errors which may be innocently committed, and to stress the need for adequate data on which these methods might usefully be employed. Although the use of figures from widely different sources means that the results must be interpreted with extreme caution, they represent what is perhaps the nearest numerical approach to the selected problem at the present time. In view of the somewhat artificial content of the illustration, it should be said that the author's intention is to demonstrate a principle rather than to try to replace clinical judgment by mathematics.

Example 1: Age of Onset

One of the facts elicited early in any patient's history is the age at which symptoms first began. From this knowledge alone, an idea of the likelihood of the diagnosis may be gained. A case may be postulated in which a patient in the late twenties develops obsessional symptoms for the first time. Although obsessional symptoms are dominant, there is a depressive affect, and the patient's pre-morbid personality is schizoid. For the purposes of this illustration, the less common diagnostic possibilities such as organic causes and mania have been ignored, and attention has been concentrated on the relative expectation of developing schizophrenia, depression or obsessional neurosis in the circumstances postulated. Table II shows the distribution of patients suffering from one of each of these illnesses, according to the age of onset. The figures for schizophrenia are those of Kraepelin (1919), those for depressive illness were found by Slater (1938), and the distribution for obsessional neurosis was given recently by the author.

TABLE II
Relative Distributions of Patients According to Age of Onset of Illness Specified

Age (years)				Schizophrenia Per cent.	Depression Per cent.	Obsessional State Per cent.
0-20	..	..	..	27.9	2	25
20-30	..	..	..	48.3	12	38
30-40	..	..	..	18.0	19	22
40-50	..	..	..	4.5	22	8
50-60	..	..	..	1.3	22	3
60-	..	..	..	0	23	4
				100	100	100

Assuming that these statistics were derived from one single general population, one can determine the relative frequency of occurrence for any age group by calculating the product of the percentage of patients beginning their illness at that age and the figure for relative frequency of occurrence of the illness in practice regardless of age. However, these illnesses do not all present obsessional symptoms at the start with equal regularity, and in order to take this factor into account, the product mentioned above should be multiplied by a figure for the relative frequency with which the three diseases show obsessional symptoms at the onset. Estimates for this last comparison vary, but Rosen (1957) found that of 848 schizophrenic patients, 17 (2 per cent.) showed obsessional symptoms at the onset; Lewis (1934) found 21 per cent. of 61 patients with depression showing obsessional symptoms, and it may be assumed that all patients with obsessional neurosis have obsessions as their presenting clinical feature.

Table III gives the data so far mentioned, including the product of the three percentages referred to. This product gives a rough estimate of the likelihood of the hypothetical patient's illness being obsessional neurosis, schizophrenia or depression.

TABLE III

Illness				Obsessional State	Depression	Schizo- phrenia
Incidence of onset of illness in age group						
20-30 years (per cent.)				38	12	48.3
Percentage of cases showing obsessional						
symptoms at onset				100	21	2.0
Relative frequency of occurrence in out-						
patients (per cent.)				2.5	23	9.1
Product:						
Approximate expectation of symptoms						
being due to illness specified				9,500	5,796	880

From this it appears that a patient between 20 and 30 years of age, regardless of sex, with dominant obsessional symptoms at the onset of a recent illness would be most likely to be suffering from a true obsessional state. In fact the "odds" are roughly 10 to 1 against schizophrenia but only 2 to 1 against depression. Although this has exemplified the faulty use of data, and the result is mainly of mathematical interest, the principle is one which if applied appropriately could bring forward conclusions of significance.

Example 2: Conclusions Drawn from Periodicity

A prominent measurable feature of any illness is its periodicity. Other factors apart, there is probably a continuous gradation between purely reactive illness, the onset of which is associated with environmental cataclysms (e.g. some hysterical conversion reactions), and apparently endogenous disease which occurs temporally connected with physiological cycles such as menstruation (pre-menstrual tension and depression). Whereas in the former example, a study of periodicity alone might be fruitless, knowledge of the phasic course in the latter case would be pathognomonic.

The next illustration shows the importance of periodicity in differential diagnosis and discusses the difference in course of manic-depressive psychosis and obsessional states which, as Lewis (1946) remarks, have been diagnostically classified together by some authorities. The author's finding was that roughly 50 per cent. of patients with obsessional neurosis had had past episodes of obsessional symptoms followed by recovery. Table IV shows the proportions of obsessional patients and manic-depressive patients according to the number of attacks of the respective illness. These figures for manic-depressive illness were given by Rennie (1942).

TABLE IV
Proportion of Patients with One or More Attacks of Illness Specified

Number of Attacks							Obsessional Neurosis	Manic Depressive Disorder
One	..	..	..	..	..	..	68 (47%)	21 (10·2%)
Two	..	..	..	..	..	..	44 (30·4%)	79 (38·0%)
Three	..	..	..	..	..	..	18 (12·4%)	63 (30·3%)
Four	..	..	..	..	..	..	12 (8·2%)	45 (21·5%)
Five	..	..	..	..	..	..	3 (2·0%)	— —
Total							145 (100%) Patients	208 (100%) Patients

As might be expected, the greatest number of obsessional patients experienced but one attack, whereas the majority of manic-depressive patients had two or more. Regarding length of attacks, there was much greater similarity between these disorders in that the majority of obsessional attacks lasted less than a year, the average length of manic-depressive attacks being estimated at 6 months (Mayer-Gross, Slater and Roth, 1954). However, the previous attacks of obsessional symptoms were in all cases followed by a more lengthy main illness and an approximation of the duration of this in 150 cases showed an average of 12½ years, this being much longer than the average manic-depressive bout. A further distinction was clear in that no less than 91 of the 141 previous attacks (65 per cent.) studied in obsessional patients occurred before the age of 20, whereas Slater (1938) discovered only 2 per cent. of first manic-depressive attacks beginning before that age.

Example 3: Pre-morbid Personality

A final illustration of the clinical application of results of natural history studies concerns the importance of pre-morbid personality. This is justifiably part of the field considered in that it is the "soil" itself and one of the many variables which influence the development of illnesses. One facet which might be reviewed again is the relationship of personality to mode of neurotic breakdown. Despite the statements by authorities such as Freud (1931) and the fact

that views are widely held that the neurosis is, as it were, an augmentation or caricature of the personality, the relationship does not appear to be so simple. The subsequent analysis, which is part of a study of obsession, attempts to shed light on one aspect of this large problem.

Freud's view was that obsessional neurosis is the pathological reaction *par excellence* to which anancastic characters are particularly liable. On common-sense grounds it would appear reasonable to suppose that the "obsessive" person (Ziehen, 1912) should be more likely to develop obsessions when he becomes ill. In fact, although many obsessional neurotics have an obsessional pre-morbid personality, not all are anancasts, and some seem to have been free of such traits in material concentration. Rüdin (1953) found among 109 patients with obsessional neurosis 67 showing traits of over-conscientiousness, pedantry, inhibition and shyness, 11 who had compulsive traits in childhood and 31 who had never shown obsessional traits before their illness. The author, selecting from a total of 150 patients those in whom sufficiently full evidence of previous personality was available, found that in 115 cases 34 per cent. showed no obsessional traits before their breakdown. Even if these figures must be accepted with caution, the finding of a fair proportion of obsessional neurotics with an obsessive pre-morbid personality does not suggest more than that personality is one factor determining the pattern of the subsequent obsessional neurosis since a considerable proportion of the general population at all social levels shows obsessive traits which are often an asset to themselves. Further disclaiming evidence is that the obsessional personality is found linked with a number of other psychiatric and psychosomatic phenomena such as depressive illness (Lewis, 1934), anxiety states, the unreality syndrome (Shorvon, 1946), anorexia nervosa (Palmer and Jones, 1939), migraine (Elkington, 1946), and duodenal ulceration (Gainsborough and Slater, 1946).

It is in connection with depression that statistical investigation is most telling. Lewis (1936) found anancastic features in the pre-morbid personalities of a third of his depressed patients. The incidence for depression in psychiatric practice may be taken as roughly 25 per cent. (p. 11) which is approximately that found by Watts and Watts (1952), but the incidence of obsessional states in a total psychiatric population of 6,230 cases was found by the author to be only 3 per cent. Even if every obsessional neurotic, but only a third of the depressed patients, had an anancastic character, the proportion of depressed to obsessional sufferers with this character would be in the proportion of 8 to 3, suggesting that anancasts are far more liable to fall ill with depression than with obsessional neurosis—this being a conclusion at variance with many strongly held views.

Example 4: National Efficiency

So far the discussion has centred on points of clinical interest, but another aspect to which natural history may contribute is that of the effect of a disease on the nation. Nowadays it is insufficient merely to know how many patients suffer from an illness and for how long mental illnesses collectively keep men off work. Further analysis is desirable to assess which social or income groups are affected chiefly, for example: Are manual workers or executives the main sufferers? Is intelligence related to incidence? In addition it is material at what time of life the illness strikes and whether individuals succumb during the active striving periods of life, in their prime or after their main work has been achieved.

The degree of incapacity borne by the individual is a starting point for wider studies such as the strain taken by relatives. For example, the parents are those mainly concerned with the anamnesis and after-care of the young schizophrenic, the spouse is often affected by the obsessional breakdown occurring in a patient in the thirties, and the children may bear the brunt of a parent's senile illness.

Other important aspects are the hospital services needed to deal with a given illness, the need for long or short term in-patient care and whether admission to hospital will be recurrent, regular or irregular. The necessity for legal intervention may be measured, giving an impression of the need for certain types of hospital and administrative services. For example it might be asked what proportion of depressed patients requiring hospital admission could be treated in general hospitals? Out-patient treatment needs could be assessed in terms of realistic economy, bearing in mind the expense of psycho-analytical methods contrasted with physical methods and their relative efficacy in relation to certain diseases. A natural history study may show whether the patient's after-care is likely to rest mainly with the family, the general practitioner, the social services, hospital out-patient clinics, or the occupational therapy or industrial rehabilitation unit. Natural history in the medico-legal field such as further comprehensive study of the lives of murderers, psychopathic personalities, alcoholics and homosexuals, difficult though a longitudinal approach would be, would provide data essential for the allocation of adequate means of management and possibly a foundation for new legislation.

A total picture of the administrative needs of any illness and its damaging effect on national efficiency should help to guide research along the most valuable lines, and avoid the misuse of services already set up, and should lead ultimately to the adoption of prophylactic measures.

ESSENTIALS OF STUDY OF NATURAL HISTORY

To enable the clinical psychiatrist to utilize the results in the consulting room and hospital, and to ensure a firm foundation for the study, the disease entity selected should be sharply defined in commonly-used terms. Perhaps the safest plan is to select a well-known entity and to describe the criteria used to amass the case material.

The research worker in clinical psychiatry is rarely able to select existing records for ideal use. In natural history studies much of the detail of the onset, course and aetiological factors are to be found in orthodox records, but in certain aspects, such as prognosis, the research worker or his team must carry out additional investigations. For this reason, under present research control, the project must be limited to the bounds of practicability. At the other extreme, the design of the research should not be restricted to the easiest route producing early results. The hitherto "cast-iron" data taken as a statutory duty from cases admitted to mental hospitals—so readily tapped and so easily to hand—rarely allowed conclusions of wide significance to be drawn from them.

Having defined the manifestations under review, a sample large enough for statistical evaluation must be obtained, the actual size of the sample being determined by initial mathematical calculation, taking into account the frequency of the included variables. This sample should be drawn from a general population whose psychological character, racial history, social and working conditions are known. The difficulties involved in proper representation in the sample of the whole of a large population may be avoided if a small

geographical unit can be adequately explored. Here again the restricted value of the result must be taken into account. Unfortunately the large samples of patients and records available in mental hospitals rarely provide representation, in so far as the illnesses are severe. Further, the indications of recovery are vague and often no follow-up is taken. Perhaps the most recent example of a satisfactory solution of this problem is shown by the masterful exposition by Hollingshead and Redlich in their study of social class and mental illness (1958).

If a group of workers are employed in the research, agreement on the factual criteria to be observed in selection of cases and collection of data should be reached early; if necessary after a pilot study. Particular care is required to ensure that all the factors needed to reach firm conclusions are investigated in a sufficient number of patients. The choice of these facts depends mainly on what is already known of the illness from clinical experience and from the results of similar earlier studies aiming at natural history.

The techniques useful in ascertaining clinical facts in follow-up studies have been fully discussed by psychologists who have been concerned with the difficult problem of assessing the beneficial effects of psychotherapy or analytical treatment. Although the ideal is to interview both the patient and a reliable informant, this method does not replace others less exacting; it does, however, safeguard against many errors. Other sources of information are postal questionnaire replies, social workers' reports, out-patient and in-patient case-notes, the patient's general practitioner, the in-patient and out-patient medical and nursing staff, and other psychiatrists who have attended the patient. In practice every source is utilized and the research worker decides which are the most valuable objectively. A popular method of beguiling simplicity, the postal follow-up, has been criticized by Lewis (1936), Berg (1952), Watson (1952) and Woodside (1953) among many others. There is however something to be said for the method used alone or to gain additional information. It is only in certain aspects of the study that the method falls short, for example in prognosis of patients whose illness has caused intellectual deterioration, and for estimating the present mental state. Woodside (1953) drew these conclusions: "That the information obtained is subjective and coloured by the patient's mood, that it is affected by the concentration of abnormal social personalities likely to be found in a psychiatric patient group, and that the stigma attached to mental disorder may lead a patient to resent a reminder of a previous breakdown." She adds that the questionnaire method cannot compare with more profound studies but it does give a general impression of the whole scene; also that in a large survey the psychiatrist may have to compromise between giving personal interviews and adopting a practicable method. Perhaps the greatest factors promoting the success of a questionnaire are its design and the patients to whom it is sent. A combination of a simple factual series of interesting questions and a group of neurotic, preferably obsessional patients, might be expected to produce satisfactory results. A pilot study quickly reveals whether or not the method will be valuable. The validity of the questionnaire may be measured if the results given by a group of patients (unknown to the investigators) are subsequently checked by personal interview. In general it might be said that the questionnaire method will be of use provided that certain groups of patients are not assessed on this alone, these being post-leucotomy cases, compensation neurotics, alcoholics, addicts, psychopaths, deteriorating psychotics and those with organic states.

Having elicited the facts from a representative sample of patients, statistical

analysis is undertaken so that the results may be appreciated readily and applied in practice. The standard tests are usually sufficient to enable concise and accurate expression of the conclusions so that the final step of building up a picture representing the temporal and quantitative features of the disorder can be taken.

Two aspects mentioned earlier require special treatment, these being aetiological factors and prognosis. The first principle in studying prognosis is that the whole of a representative sample of patients should be traced. Very often there is difficulty in tracing patients some years after they have finished formal treatment; the sample then fails to be representative and bias is introduced. This difficulty is enhanced by the operation of another desirable principle—that follow-up should be as long after the beginning of the illness as possible to allow for the slow-moving but inevitable changes seen in mental illness. Thus the task of conducting a proper follow-up study may be arduous, although the fascination of a profound study of this kind has been encouragingly exemplified in the accounts given by Partridge (1950) and by Pippard (1955) of their studies of widely distributed leucotomized patients.

In the assessment of aetiological factors, all preconceived notions are set aside. Only if this is done can the *post hoc ergo propter hoc* fallacy—foremost in some analytical theories—be avoided. Perhaps there is no realm of mental illness in which the inexperienced find more difficulty in keeping an open mind than in that of aetiology. Yet in psychiatry, of all specialities, there are few illnesses whose aetiology is proven. To attack this problem it is essential to find those factors operating before the earliest manifestations of the illness itself for, as in neurological cases, so often a cataclysmal event is a consequence of the disordered psyche rather than its cause. Only facts can be utilized, for as Straus (1948) has remarked: "The unconscious thoughts of patients are nothing more than the conscious opinions of their physicians".

THE NATURAL HISTORY OF OBSESSIONAL STATES

This section gives the results of the author's attempt to study the natural history of an illness which has attracted the interests of psychiatrists to a considerable degree. Obsessional neurosis was selected because of the somewhat hesitant statements about it in current textbooks, and the dearth of comprehensive data, especially regarding prognosis. Full statistical detail, extended treatment of certain aspects, pre-morbid personality and precipitating factors, and case histories have been omitted for the sake of brevity.

For this investigation, an obsession was defined as "a recurrent or persistent thought, image, feeling, impulse or movement, which is accompanied by a sense of subjective compulsion and a desire to resist it; the event being recognized by the individual as foreign to his personality and into the nature of which he has insight". An obsessional illness or state was regarded as one in which obsessional symptoms were dominant, there being no other recognized mental reaction responsible for them, and for which the patient sought medical advice. There was no evidence to suggest an organic aetiology for the symptoms in those selected for study.

1. Method of Selection and Case Material

The case material was chosen from the total patients admitted to the psychiatric in-patient unit of a London hospital over a period of eight years, and from the whole of the patients seen privately by a consultant psychiatrist.

Of the 150 patients chosen, 69 had been in-patients and 81 had been seen privately as "out-patients". The hospital patients comprised 18 (26 per cent.) males and 51 (74 per cent.) females (a larger number of female beds being available during the relevant admission period). The private "out-patients" included 45 (55.5 per cent.) males and 36 (44.5 per cent.) females.

Information was collected from case records, from reports kindly sent by other psychiatrists and from data provided by social workers, and the medical and nursing staff. When possible, patients and their relatives were seen personally. After modification in the light of a pilot run, a specially designed questionnaire was sent to all patients. In the assessment of each case all available sources of information were used, but in no instance was a favourable outcome assumed on the basis of a postal reply alone.

2. Age of Onset of First Symptoms

Owing to the periodicity shown by the course of the illnesses studied, the age when first symptoms began was distinguished from the age of onset of the main illness. Table V shows the distribution of 141 patients according to the age at which they experienced obsessional symptoms for the first time.

TABLE V

Age Group (years)										Number of Patients Developing First Symptoms
6-10	..	..	..	..	..	..	..	..	..	22
10-15	..	..	..	..	..	..	..	..	..	25
15-20	..	..	..	..	..	..	..	..	..	27
20-25	..	..	..	..	..	..	..	..	..	22
25-30	..	..	..	..	..	..	..	..	..	14
30-35	..	..	..	..	..	..	..	..	..	11
35-40	..	..	..	..	..	..	..	..	..	10
40-45	..	..	..	..	..	..	..	..	..	6
45-50	..	..	..	..	..	..	..	..	..	0
50-55	..	..	..	..	..	..	..	..	..	1
55-60	..	..	..	..	..	..	..	..	..	0
60-65	..	..	..	..	..	..	..	..	..	1
65-70	..	..	..	..	..	..	..	..	..	1
70-75	..	..	..	..	..	..	..	..	..	1
Total	..	..	..	..	..	..	..	..	..	141

In 68 patients who had no previous attacks, the first symptoms constituted the present illness. The majority of patients (68 per cent.) experienced their first symptoms before the age of 25, and only four after 45 (2.7 per cent.). As age increased above 20 years fewer and fewer individuals developed symptoms for the first time. The mean age when first symptoms came on was 21.6 years in females, and 20.2 years in males; there was no significant sex difference.

3. Earlier Attacks

Frequently patients' histories revealed that attacks of obsessional symptoms had occurred before the main illness, each attack ending in apparent recovery. Of the 150 patients, 100 had reported such earlier episodes and 82 of the latter had sought medical advice at the time. These 82 individuals had experienced between them 162 attacks, the average number of attacks per patient being roughly 2, but the extremes were 1 and 10 attacks. Regardless

Three-quarters of the patients were incapacitated before the age of 40. Approximately half broke down within a year of the onset of symptoms forming the main illness, but the remainder were incapacitated only after a considerable number of years had elapsed. The mean duration of the main illness before the patient was disabled was 4.7 years.

6. *Endurance of Symptoms*

An estimate of the period of suffering in the main illness before each patient was seen for the first time privately or at hospital showed that of 150 patients, approximately half attended within two years of the onset of symptoms and nearly a quarter were seen after 10 years. The average period between onset of the main illness and attending for advice was 7.5 years.

7. *Prognosis*

Altogether 101 patients were followed up by one or more of the methods enumerated earlier. The length of follow-up from the time patients first attended for advice was between 3 months and 15 years (mean: 3.5 years). A simple rating scale, similar to that given by Müller (1953), was used to classify the patient's state of adaptation viz.:

Group 1: Patients who were socially adapted and symptom-free.

Group 2: Those who were socially adapted but still experiencing mild symptoms.

Group 3: Those who were poorly adapted socially but whose symptoms had improved.

Group 4: Those whose symptoms were worse or as severe as when they were first seen.

Group 5: Those whose obsessional symptoms had been replaced by other phenomena.

Table VIII shows the patients distributed in these groups at the end of the follow-up, leucotomized cases being separated for this analysis.

TABLE VIII
Group

	1	2	3	4	5	Dead	Suicide	Total
Leucotomized ..	15	6	7	5	0	0	1	34
Non-leucotomized	16	24	8	17	1	1	0	67
Total (patients)	31	30	15	22	1	1	1	101

Two-thirds of those followed reached a stage of social adaptation, half of them becoming symptom-free.

To define more closely the results after a definite period, and to allow for the periodic course noticed, Tables IX and X show respectively the patients' state after one or more, and after four or more, years from the time they first sought advice.

TABLE IX

		Group					Total (Patients)	
		1	2	3	4	5		
Leucotomized ..	..	..	12	6	7	4	0	29
Non-leucotomized ..	..	..	19	18	6	9	1	53
Total ..	..	..	31	24	13	13	1	82

TABLE X

				Group					Total (Patients)
				1	2	3	4	5	
Leucotomized	..	..	..	4	4	4	3	0	15
Non-leucotomized	..	..	..	12	9	3	5	1	30
Total	..	..	..	16	13	7	8	1	45

Of the small sample of patients reviewed after four years, two-thirds of those not leucotomized were socially adapted and over half of these were free of symptoms.

8. Factors in Prognosis

In view of the very few prognostic factors described in the literature, an attempt was made to relate some of the variables estimated to the patient's progress.

It might be expected that the beginning of obsessional neurosis early in life would be associated with a poor prognosis. In fact, no significant difference in age of onset was found between those who did well and those who did badly. This result agrees with Müller's opinion that no prognostic conclusion could be based on the age at which the illness began.

Straus (1948) described two groups of obsessionals according to outcome. The first group noticed a sudden onset of symptoms in the third decade or thereabouts and showed a good prognosis; the second group with continuous development from an early age tended to reach a state of severe invalidism. However, among the 150 patients in the present series, very few noticed a sudden onset and only one of these was found to have a good outcome. Müller (1957) found that all his patients described an insidious start to their symptoms.

The fact that patients had had previous attacks appeared to affect the prognosis favourably, but there was no association between the number or length of such attacks and prognosis. However, the finding of a good prognosis in those showing a phasic course may be due to the greater chance of reviewing such patients in a remission. Further, a phasic course suggests that future episodes may occur and from this point of view the outcome is poorer. The conclusion reached was that a past history of previous episodes of symptoms could not be used as a prognostic guide.

Partridge (1950) found that obsessive-compulsive rumination yielded more readily to pre-frontal leucotomy than did ritualistic behaviour, but an analysis of the present series showed no significant difference in prognosis between the ritualists and non-ritualists who did not undergo neurosurgical treatment. This may be due to the fact that patients not operated upon had milder forms of illness.

Pre-morbid personality did not influence the outcome of obsessional illness to the degree expected. Although the number of patients assessed was small, the only significant finding was that there were more individuals with few obsessional traits (as opposed to those with many such traits or alternatively no traits) in the group of patients who fared well.

The most profound influence on prognosis was the duration of the obsessional state before the patient sought psychiatric advice. The mean duration of the illness until the patient was seen privately or at hospital was 3.0 years in those who became symptom-free, and 8.1 years in those who

showed no improvement at the end of the follow-up. The patients with a good prognosis were seen after a significantly shorter period of suffering than were the patients with a poor prognosis ($P=0.05$). Further evidence to support this finding was obtained from estimation of the total duration of the illness in those patients with a good prognosis, i.e. those who became symptom-free or socially adapted (Table XI). Over half the patients who did well had less than 5 years of illness and less than a quarter had more than 10 years. The longer the duration of the illness the fewer patients were found to have recovered.

TABLE XI

Duration of Illness (years)									Number of Patients Recovered or Improved
0- 2	..	..	..	..	..	..	..	..	22
2- 5	..	..	..	..	..	..	..	..	15
5-10	..	..	..	..	..	..	..	..	11
10-20	..	..	..	..	..	..	..	..	7
20-40	..	..	..	..	..	..	..	..	6
Total	..	..	..	..	..	..	..	..	61

CRITICISM

The chief criticisms of this study of obsessional states centre on the problems of sampling and the investigation technique, but it should be said that the technique adopted was a compromise between a recognized ideal and what could be accomplished with the facilities available.

The size of the sample was adequate for most purposes such as the study of the onset of the main illness, previous attacks, age of breakdown and age at which psychiatric advice was sought; this was so because relevant information was available about a majority of the individuals in these respects. For the follow-up however, only two-thirds of the original group could be traced, and only in a fraction of this number could an assessment after a reasonable period be effected. This circumstance illustrates the importance of amassing a substantial sample initially, for even the most zealous investigator must expect to miss a proportion of the total material in the follow-up. To report only on patients traced and followed and to ignore those lost is merely to create a false impression, and it is undoubtedly better to qualify the results of a partial study rather than present the misleading results of an apparent 100 per cent. follow-up on a smaller group. Further, some guide to the prognosis of those untraced can usually be found in the case notes based on the original clinical investigation. Although large samples of obsessional states are desirable for study, the comparative infrequency of their occurrence (3 per cent.) means that a sample of 300 patients would require a total patient population of 10,000 from which to select. Undoubtedly this factor must have accounted partly for the dearth of large-scale studies in the past.

The second aspect of sampling was the problem of representation of all forms of severity of obsessional neurosis. The series contained a majority (54 per cent.) of "out-patients" with milder illnesses and, as 31 of the hospital patients with more severe states were leucotomized, the remainder (38 patients) did not equal the many milder cases included. This resulted in a bias towards milder illnesses in those patients used to demonstrate the natural outcome. Another bias was in favour of the female sex, females predominating in the sample (87 females, 63 males). This ratio was apparently brought about by

administrative factors in that more female beds were available for admission during the relevant period. If in fact females are more liable to develop obsessional states than males, it might be justifiable to ignore the detailed distribution, but the findings of other workers vary. Janet (1903) remarked on the considerable preponderance of females in his cases of psychasthenia among which were 230 females but only 95 males. Terhune (1949) in a series of 86 patients with phobic reactions found women twice as frequently as men; women predominated in Rüdin's large group of in-patients and out-patients (1953). Müller (1953), however, in a series of 57 obsessionals, discovered the inverse proportion (20 females, 37 males). In the absence of convincing reports, the figures for the present study must be assumed to over-represent the female sex.

Another influence affecting this sample was social class or income group. Lewis's view (1936) was that the obsessional patient's characteristic insight had misled many authors to assume that such individuals were of higher intelligence than average. There are, however, independent observations by a number of writers which suggest that patients suffering from obsessions are more likely to be found amongst more gifted, more intelligent and more energetic folk. Morel (1866) noted that intellectuals and those of the professional classes were more likely to suffer from obsessions; Stekel (1950) wrote that compulsion neurotics were frequently intelligent, gifted persons, even people of genius; Gruhle (quoted by de Boor, 1949) found that obsessions were usually manifest in more differentiated personalities or those with high intellectual standards; Müller (1953) also found obsessionals to be gifted, versatile and energetic. Similar views have been expressed by Bleuler (1924), Jelliffe and White (1935), Woolley (1937) and Schneider (1958). The recent statistical study by Hollingshead and Redlich (1958), however, shows convincingly that obsessional illnesses are progressively more frequent with ascent in social class, and it may be that the sample used for this study was truly representative in this respect.

Other difficulties in studying the present group of obsessionals concerned the follow-up technique. The time and facilities available did not allow for a personal interview with each patient and a relative, but all other sources of information were tapped, the final assessment of a patient's state at the end of the follow-up being a subjective judgment based on these. The actual sources were as follows:

<i>Direct:</i>	Personal interview with patient.
	Personal interview with relative or informant.
<i>Indirect:</i>	Out-patient notes and opinion of physician.
	Social worker's report.
	General practitioner's report.
	Report from other psychiatrist or hospital.
<i>Purely</i>	Replies to routine, periodic, hospital questionnaire.
<i>Documentary:</i>	Replies to specially designed questionnaire.

In the following table, the patients are shown distributed according to their follow-up category (p. 26) and the best source of information available.

Undoubtedly, the weakest method used was the postal follow-up, the defects of which have already been mentioned briefly. Subsequent detailed

TABLE XII

						Best Source of Information		
						Direct	Indirect	Documentary
1	..	..	..	..	..	7	24	0
2	..	..	..	..	..	7	19	4
3	..	..	..	..	..	8	5	2
4	..	..	..	..	..	5	9	8
Totals	..	..	..	..	..	27	57	14

98 patients

analysis of the questionnaire replies from patients showed that there was a high degree of internal consistency in answering, and that in those cases where objective evidence was later obtained, the degree of accuracy in replying was also high. In the light of Woodside's (1953) remarks on the poorer quality of answers by sociopathic individuals, it is perhaps in the obsessional group that the results are most likely to be reliable. An observation by Miles, Barabee and Finesinger (1951), on what might be a less reliable group, is of some interest. They found in a series of patients with anxiety neurosis that the patients' evaluation of their states correlated highly with the psychiatric assessment (0.79). Against this evidence must be set the secretiveness of the obsessive character, stressed by Laycock (1845), Freud (1907), Stekel (1950) and Rosen (1957); this may be one explanation for the long delay between the onset of symptoms and the patient's attendance for advice (p. 25). In fact in the present series, no patients were assumed to be symptom-free on the basis of their postal replies alone. Although the follow-up period seems comparatively short (3.4 years), the average duration of illnesses suffered by the patients at the conclusion of the survey was 12.5 years, so that the results cover a much longer period of illness evolution.

SUMMARY

Bearing in mind the qualifications applying to the work, certain conclusions were reached from the findings in this study of the natural history of obsessional neurosis.

The incidence was low in psychiatric practice, being less than 5 per cent. in both private and hospital cases and in both sexes. The figures compare favourably with those of Terhune (1949) and Müller (1953) and give some indication of the degree of selection employed.

The age of onset of first symptoms was roughly equal in both sexes, and in the majority of patients it was before the age of 25. After 20, the risk of developing obsessional symptoms decreases with increasing age. Müller's report suggests a similar age distribution to the present, and although Freud (1913) declared that the first symptoms of obsessional neurosis declare themselves between 6 and 8 years of age, most obsessionals seem to date the onset later.

Half the patient's illnesses showed a phasic course with an average of two attacks before the main illness. Two-thirds of these attacks began before the age of 20 and 90 per cent. before 30. These episodes were usually short (79 per cent. lasted less than a year) and clinical recovery apparently followed. The periodicity of the attacks differed from the course of manic-depressive illnesses in general in that the attacks occurred during early life and in all cases they were followed by a prolonged illness. Obsessional symptoms occurring before

the age of 30 often have a good prognosis and this should be borne in mind when considering leucotomy.

The main illness occurred during the active, striving periods of life between the ages of 10 and 45 in the majority. After the age of 30, the risk of developing obsessional neurosis diminished with increasing age, and the decreasing attendance in higher age groups is suggestive of improvement in some patients. The importance of these facts reported earlier by Janet (1903) and Greenacre (1923) has not been widely stressed in relation to the differential diagnosis of obsessional symptoms, although Lewis (1938) warned of the increased liability of organic aetiology for obsessions beginning in later life. In summary, the late onset of obsessions should lead to the exclusion of organic causes and other mental reactions before obsessional neurosis is diagnosed.

Three-quarters of the patients were disabled before they were 40; only 10 per cent. after 50. Supporting, in some respects, Pavlov's (1941) dog-human analogies, these patients showed considerable temporal resistance to breakdown since the average period of the main illness before advice was sought was 4·3 years. This delay might be partially explained by the patients' secretiveness, but curiously enough Hall (1935) found that there was a similar delay in sending children with obsessions for investigation; often 2 to 5 years elapsed before the condition was recognized.

The follow-up showed a less gloomy picture than many painted in textbooks. The findings suggested that a third of obsessional patients will become free of obsessional symptoms or reach a stage of social adaptation at least for a period of time. If the bias produced by failure to trace all patients could be ignored, it can be said that two-thirds of a large group of obsessional neurotics will become socially adapted and that half of these will be free of symptoms.

The following table shows earlier results in rank order according to increasing bulk of the samples. For this comparison, the possibility of recurrence of the illness has been ignored.

TABLE XIII

Author			Date	Sample Size	Length of Follow-up	Percentage of Cases with Good Prognosis
Rüdin	..	..	1953	130	2-26 years	39
Müller	..	..	1953	57	15-35 years	49
Lewis	..	..	1936	50	5 years and over	56
Hastings	..	..	1958	23	6-12 years	44
Yaskin	..	..	1936	13	—	50

These results are based on different populations in that Swiss, German, North American and British patients have been separately sampled. If the lowest finding in the present series is added, and the number of patients with a good outcome in all the samples is calculated as a percentage of their joint total (374), the figure of 43 per cent. is obtained. This overall estimation helps perhaps to neutralize many of the differences between samples, follow-up length and technique, and might be used clinically as a prognostic guide.

Investigation of prognostic factors in the present series was disappointing but it was concluded that the most favourable prognosis depended on the duration of illness before the patients were seen, those seen within a shorter time of the onset having a better chance of recovery, regardless of the actual age of

beginning the illness. In addition, patients with obsessive personalities seemed to do better than those with either anancastic or non-obsessional characters.

CONCLUSION

The importance of a thorough case history has long been realized in general medicine, and credit for the most recent and broad emphasis of this need in psychiatry is due largely to Adolf Meyer. Although clinical psychiatry has developed extensively, it is suggested that natural history studies of many reactions—classical and atypical—are an additional but virtually untapped source of information which could play an important role in diagnosis, management and many other aspects of clinical and administrative psychiatry.

Nowadays, since the introduction of more effective methods for treating some of the commoner illnesses, psychological medicine is thriving on a practical basis. We should not, however, allow our enthusiasm for the purely therapeutic approach to blind us to the need for a better understanding of the full range of psychological abnormalities. By establishing the broad principles of their natural evolution we may more readily decide upon the best methods for their prevention, alleviation and cure.

It is submitted that the results of the present enquiry, based on a study of the natural history of one of these illnesses, the obsessional neurosis, indicate a sound means of achieving our aim.

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THE POSSESSION SYNDROME: A COMPARISON OF HONG KONG AND FRENCH FINDINGS

By

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THE phenomena of "spirit-communication" in mediumistic trance, of "spirit-possession" and of "demonopathy" are closely related, and known to both East and West. Clinical psychiatrists, however, have taken little interest in them, with the exception of some French and a few Spanish authors. These conditions nevertheless do present themselves to the psychiatrist in many countries and it is misconceived to think that they are to be found only in outlandish cultures, the preserve of the field worker in ethnology. It is true that M. J. Herskovits (1951, 1958) has argued that certain kinds of behaviour categorized in terms of culture-bound concepts cannot be applied to other societies, so that African and Afro-American spirit possession, for example, cannot be compared with apparently similar "psychopathological seizures" in the West. No doubt such behaviour receives different cultural definitions according to their respective backgrounds, but this does not exclude the possibility of a specific psychological mechanism being common to them all.

This paper examines the possession syndrome as it is manifested in patients coming to the Mental Hospital in Hong Kong and compares the findings with those described in the literature for French Catholic patients. It attempts also to show how the condition can be better understood by reference to the cultural and socio-economic background, and by the application of certain psychological concepts commonly associated with the names of G. H. Mead and H. S. Sullivan.

REVIEW OF LITERATURE

The psychiatric literature on demonopathy is almost entirely confined to the French and behind French contributions there is a long tradition. Discussion of "Cotard's syndrome" has from the beginning linked it with possession (cf. H. Ey, 1950). Leroy and C. Portier (1930) discussed spirit possession following the practice of spiritualism and gave a striking quotation from Lévy-Valensi: "*Le salon spirite est, pour certains, l'antichambre de l'asile*". They accepted the classification of Cl. Vurpas who divided cases into the acute and curable, and the chronic and incurable. J. Vinchon (1931) distinguished three types of possession: those arising from Ségla's contrast obsessions and Clérambault's dissociative process; anxiety nightmares leading to a psychotic picture, due to sexual conflict; and hysteria conditioned by excessive imagination and contact with the old demonology and theosophy. P. Schiff and R. Simon (1933) described

the case of a young post-encephalitic woman with pseudocyesis who, after the expected labour had failed to take place, became deluded that she was possessed by an animal spirit. J. Delay (1945) published the case of a man suffering from agitated melancholia and showing contrast obsessions; he pointed out that in this case the fear of possession led to his being possessed, the intellectual possibility leading to affective certainty. He also mentioned the finding of G. Gayral that seven out of ten cases of possession were melancholic. L. Mars (1946) studied cases in Haiti and implicated "*un processus schizonoïde d'apparence mystique*"; possession he regarded as associated with the gregarious and Dionysian aspects of religion and he thought it provided a cathartic mechanism for maintaining mental health. L. Michaux, H. M. Gallot and J. C. Dubois (1947) described the condition in an alcoholic male and pointed to the operation of several factors: the absence of oneirism and mental confusion, which factors normally favour the development of coherent delusions; the intensity of psychomotor and coenaesthetic hallucinations, which, like all alcoholic hallucinations, have an imperious quality about them; and the utilization of a complex springing from unconscious remorse. M. P. Giscard (1948) attempted a comparison between the stages of possession and of *grande hystérie* and claimed that somatic phenomena like subcutaneous haemorrhage and oedema were to be seen in both. H. Aubin (1952) distinguished states of "pseudo-possession" in which there is no true doubling of the personality but only a morbid transformation; and pointed out that even in cases of true doubling with ideas of diabolical persecution still there may not be delusions of being possessed. M. Despinoy, R. Millon and Y. Tuelié (1953) described a case which exhibited delusions of possession alternating with exacerbations of phthisis. C. Pidoux (1955) reported on states of ritual possession in Africans, emphasizing their normality within their own cultural context.

The work of J. Lhermitte (1944, 1946, 1955, 1956) reveals him as an outstanding authority on the subject, with considerable experience of such cases. The position he takes is that of an orthodox Catholic psychiatrist who accepts the co-operation of the exorcist. "*Le médecin qui veut rester un homme complet*", he writes, "*ne peut . . . exclure, a priori, la possibilité d'une étiologie transcendente dans la production de certains psycho-névroses, dont la source naturelle ne se découvre pas au savant*" (1956). He therefore distinguished (1955) "true possession" from "false possession", i.e., demonopathy; the former being probable where psychiatric explanation in a given case does not appear to be adequate or plausible. This point of view, it appears, is not widely held by French psychiatrists. Lhermitte's positive contributions to the study of this subject are important.

He believes (1944) that possession is a complex state, neither a nosographic entity nor a legitimate syndrome but only a picturesque coloration given to psychoneuroses like "*hystérie*", "*pithiatisme*" and "*mythomanie*", or "true psychoses" like "*psychoses hallucinatoires chroniques*" and "*automatisme mental*". He also distinguished in 1946 two types of demonopathy: one coming in attack form with clouding of consciousness, as in hysteria or epilepsy; and the other an insidious form with an understandable evolution, the patient being lucid and able to give an account of the psychological and physical aspects of the state of being possessed. The latter form he regarded as incurable. Later, in 1955, he differentiated cases of "internal demonopathy" in which the demon enters into the patient's mind and body, from "external demonopathy" in which the patient has delusions of persecution by the demon from without. He pointed out that not all cases in his experience were believers in the Catholic

doctrine and that sometimes organic causes were responsible. The importance of guilt he emphasized, especially guilt arising from unconscious homosexual trends.

The occurrence of possession (and zoanthropy) in Japanese has been noted by K. Miyake (1925), and among them the condition is usually given the name of "invocation psychosis", after the German term. T. Y. Lin (1953) briefly touched on this topic in his survey of mental illness in Chinese and mentioned the name *hsieh ping*, which however is not used in Hong Kong. E. K. Yeh (1958) described a Chinese case in whom possession alternated with urticaria. The broad historical and ethnological survey of T. K. Österreich (1930) is well-documented, but does not seriously take up the psychological approach. However, R. Linton's (1956) discussion of possession, especially those forms occurring in North America (Holy Rollers and Jumpers) and in Madagascar, is valuable for its psychopathological insight. Gordon's study of so-called "maggidic hallucinations" (1949) is interesting not only because it shows how the phenomena we are studying can be specially moulded by cultural and personality factors, but also because it contains speculations regarding nosography by a number of contemporary psychiatrists. The attempt of C. H. Thigpen and H. M. Cleckley (1957) to apply contemporary psychiatric theory in elucidating a recent American case of multiple personality should also be noted.

CLINICAL MATERIAL

Between 1954 and 1956 (inclusive) there were admitted into the Hong Kong Mental Hospital 66 men and women, all first admissions, who exhibited the possession syndrome either in pure form or else some elements of it within the content of an hysterical delirium or of some other mental illness. This number was 2.4 per cent. of all first admissions for that period, but if only the case showing the pure syndrome (see definition below) were counted the figure was 0.3 per cent.

Certain features of interest emerge when these cases are analysed and examined against the base demographic and socio-economic data for Hong Kong collected by the Hambro Sample Survey in mid-1954 (Hambro, 1955).

SEX DISTRIBUTION

In the sample, 50 cases were female and 16 male, and the disproportion in the sexes is even more marked if only the hysterical and depressed cases are considered. There is no need for statistical analysis to demonstrate that the difference in the numbers of the two sexes is significant. This finding of a great preponderance of females appears to be in contrast to what obtains among French cases, as far as can be gathered from a survey of the recent literature. The possible meaning of this will be discussed later.

AGE

Table I shows the age distribution of our sample for each sex. Analysis reveals that there is no significant difference between this and the distribution of various age groups for each sex in the general population. It is evident therefore that age does not play a part in determining the referral of cases to the psychiatrist or admission to hospital. The youngest cases were aged 16 for each sex and the oldest aged 47 for men and 60 for women.

TABLE I
Age Distribution

					Percentage in Population		No. of Cases	
Age (Years)					Male	Female	Male	Female
11-35	..	..	..	..	65.7	60.2	9	28
36-55	..	..	..	..	28.8	31.5	7	18
56-	..	..	..	..	5.5	8.3	—	4
					100.0	100.0	16	50
For males					$\chi^2=1.9$	Df.=2	$P>0.5$	
For females					$\chi^2=0.3$	Df.=2	$P>0.8$	

TABLE II
Age of Onset

Age (Years)									Male	Female
16-25	..	..	..	..	..	..	..	..	3	15
26-35	..	..	..	..	..	..	..	..	7	17
36-45	..	..	..	..	..	..	..	..	5	14
46-55	..	..	..	..	..	..	..	..	1	3
56-	..	..	..	..	..	..	..	..	—	1
									16	50

$\chi^2=0.8$ Df.=4 $P>0.9$

On admission only 2 men in our sample but as many as 15 women had had previous episodes of possession. Moreover, even taking into account age differences women tended to have more previous "attacks" than men, the maximum being 7 for the former and 2 for the latter. Table II shows the distribution of age of onset for each sex and analysis reveals that there is no significant difference between the two. Since this is so, and age has no selective effect on the admission of each sex, the fact that men have fewer previous attacks must mean that they are less prone to attacks. It is of interest to note from Table II that, while female sex predisposes to possession, it affects all ages equally.

MARITAL STATUS

Table III compares the distribution of marital status among our sample cases with that in the general population. It is found that taking both sexes together there is a significant difference between the two. Widows and widowers along with the divorced, and also concubines, were over-represented in our series, and the married and single were under-represented.

TABLE III
Marital Status

Status					Percentage in Population		Male	Female	Total
Married	..	..	..	..	60.5		5	28	33
Single	..	..	..	..	29.2		9	6	15
Widowed and divorced	..	..	..	..	9.8		2	11	13
Concubines	..	..	..	..	0.5		—	5	5
					100.0		16	50	66

Both sexes: $\chi^2=10.1$ Df.=3 $P<0.02$

That the widowed and divorced are a peculiarly vulnerable group is well-known from studies in social psychiatry; to this must be added, as far as our study goes, the group of concubines. These persons still exist as such in overseas Chinese communities in South-East Asia, but not in mainland China nor in Taiwan. I have previously shown (Yap, 1958) that concubines have an unusually high suicide rate, and evidence that they also have a high mental hospital admission rate awaits publication.

EDUCATION

Data on the distribution of educational levels in the general population do not exist, but a good idea of the specific influence of education on the predisposition towards possession can be obtained by comparing our series with the total Chinese mental hospital population as regards educational attainment (all our cases were Chinese). Data on this obtained in January, 1958, are given in Table IV. The difference between the two distributions in the table is significant, and it may be concluded that our sample includes an unduly large

TABLE IV
Educational Attainment

Education				Percentage Among In-patients	Male	Female	Total
Illiterate	..	..	..	21.5	2	25	27
Primary	..	..	..	50.3	9	21	30
Middle	..	..	..	22.0	5	4	9
College	..	..	..	6.2	—	—	—
				100.0	16	50	66
Both sexes: $\chi^2=18.1$				Df.=3	$P>0.001$		

proportion of illiterates and an unduly small proportion of the well-educated. There is no reason to suppose that the composition of our patients in hospital could have changed much between the period during which the cases were admitted and January, 1958. As for the obvious criticism that the control hospital patients would include a disproportionate number of chronic psychotic who were likely to be drawn from lower economic levels and therefore be uneducated, even if this were true it would not be a serious objection. If the mental hospital population used for comparison is biased in the direction of having among them too many illiterates compared with the general population this fact would make our finding even more significant, and strengthen rather than weaken our conclusion that lack of education predisposes towards the syndrome.

OCCUPATION AND SOCIAL CLASS

Table V gives the various occupations listed in the Hambro Survey arranged into four social classes according to the criteria of education, income and prestige. The criteria are admittedly subjective, and the abnormally rapid socio-economic changes in Hong Kong make them even more questionable, but there can be no doubt that the classification does give a fair picture of class stratification in Hong Kong. The population data in the Hambro Survey, used for control, include all those aged 16 and over, but exclude the unemployed, housewives, and a small miscellaneous group labelled "others".

TABLE V
Occupation and Social Class

Social Class	Occupations Included	Percentage in Population	All Cases*		Total* Excluding Housewives and Concubines
			Male	Female	
I	Professionals	6.6	—	—	—
II	Managers and business employers ..	4.4	—	2	1
III	Primary school teachers, clerks, students, mechanics, salesmen, taxi-drivers, policemen, telephone operators, individual merchants	12.7	3	11	4
IV	Independent and cottage craftsmen, hawkers, shop assistants, factory workers, industrial labourers, butchers, cooks, fishermen, boatmen, coolies, domestic servants	76.3	13	35	38
		100.0	16	48	43
Total, excluding housewives and concubines: $\chi^2=8.0$			Df. = 3	P < 0.05	

* 2 unemployed women excluded.

In our material 2 unemployed women were not taken into consideration. Housewives (and also concubines) might be classed as usual according to the occupation of their husbands, but this is unreliable in our case since the principle of assortative mating, based as it is on the free choice by individuals of marriage partners, cannot be held to apply fully in Hong Kong. If we exclude housewives and concubines from our series, analysis shows that occupations of low status are significantly over-represented in our sample when comparison is made with their numbers in the general population.

RELIGION

Table VI gives the religious affiliations of our cases, but it should be clearly understood that the data are not very meaningful inasmuch as the factor of firmness of belief has not been taken into account. Moreover, most Chinese adopt a syncretic rather than a doctrinaire attitude towards religion, a common saying being that "all sects have their truth and all truth its sects". Normative data on the distribution of religious affiliation in the general population are

TABLE VI
Religious Affiliation

Religion	Male	Female	Total
Taoist-Buddhist-Confucian	10	43	53
Protestant	—	3	3
Catholic	1	2	3
None professed	5	2	7
	16	50	66

lacking, but it would appear that, if the figures mean anything, there is an unusually great number of Christians in our sample, for the proportion of Christians in the general Chinese population is certainly much less than 1 out of 11 (6 out of 66). It is possible that persons taking to organized Christianity represent a selected group with strong emotional needs; or the religion from our present point of view may have a characteristic psychological effect on poorly

educated persons to whom it is new. M. J. Field (1958) has reported that certain African Christian Sects, claiming to worship after the manner of the earliest Christians, become "Pentacostally affected" *en masse*.

DIAGNOSIS

Table VII shows that the syndrome of possession, manifesting itself in varying degrees of completeness, is not a unitary one but is distributed among different psychiatric reactions. When it occurs in pure culture on the basis of an hysterical delirium it is to be found in more than half of the female cases, but in males it is seen in less than a third. The chief differential diagnosis to be considered from hysteria are schizophrenia and depression.

TABLE VII

Diagnosis

Diagnosis	Male	Female	Total
Hysteria	5	27	32
Schizophrenia	4	12	16
Depression (with hysterical features)	4	4	8
Mania	2	2	4
General paresis	1	1	2
Senile confusion	—	1	1
Lactational confusion	—	1	1
Febrile delirium	—	1	1
Post-epileptic confusion	—	1	1
	16	50	66

CLINICAL PICTURE

The state of possession was manifested in varying degree and the distribution of cases in terms of degree of completeness is shown in Table VIII. Degree 1 is characterized by clouding of consciousness, skin anaesthesia to pain, a changed demeanour and tone of voice, the impossibility of recalling the patient to reality, and subsequent amnesia. Degree 2 is characterized by mild clouding, partial anaesthesia, no change in voice and demeanour, the possibility of recall to reality, and partial amnesia subsequently. Degree 3 is marked by the absence of clouding, of anaesthesia, and of change in voice and demeanour, the possibility of immediate recall to reality and the gaining of attention, together with (in females) mannerisms like giggling, belching and other attention-seeking devices.

TABLE VIII

Degree of Possession

	Degree	Male	Female	Total
I	Complete	—	7	7
II	Partial	6	25	31
III	Histrionic	10	18	28
		16	50	66

Comparing the sexes: $\chi^2=56.7$ Df.=2 $P>0.001$

The distribution of degrees of completeness in the syndrome is significantly different between the two sexes. Females tend to manifest the syndrome in its

pure form and in fact there was not a single male case in Degree 1. Of the female Degree 1 cases, 6 belonged to the lowest of our four social classes, i.e. class 4, and only 1 to class 2; the latter was a phthisical, illiterate woman married to the part-owner of a restaurant who had lost his first wife. Only 7 out of the 66 cases showed the classical or complete syndrome, and these were all women; the diagnoses in these cases were: hysteria (3 cases), schizophrenia (2), reactive depression with hysterical features (1), and febrile delirium (1). A point of interest is that one of the schizophrenic cases became possessed only when coming out of insulin coma.

The general demeanour of the incomplete cases was variable. It included gagging, torticollic movements, chanting (often in a village *patois*), shutting of the eyes, lying stuporose on the ground, rolling about, climbing up windows, panting, somersaulting, attacking people around, scratching the tongue with the fingers, walking on the knees, imaginary throwing of rice grains about (this being a ritual of the professional mediums), etc. The more severe cases acted in a manner suggested by the nature of the possessing "spirit" or "personality". Thus there were two cases of theiromania based on possession by a fox spirit and a snake spirit of peasant folk-lore; the former barked and pawed and the latter chirped, or rather attempted half-heartedly so to do. Twenty-two cases were possessed by the spirits of dead relatives; 18 by deities of the Taoist-Buddhist Pantheon; 17 by both dead relatives and deities; 2 by culture heroes (a legendary seer and Sun Yat-sen); and 1 each by Jesus Christ, the Virgin Mary, the Christian God, an Indian Prince, and a living clairvoyant ("fortune-teller").

Clearly many of the cases could have been labelled variously as examples of hysterical delirium and twilight state, hysterical puerilism, buffoonery syndrome, pseudologia phantastica, mythomania and even playful malingering; the common element being the idea of possession held in the context of exuberant myth and legend.

In a number of cases the apparent possession was not the central content of the symptoms but the patient exhibited behaviour otherwise bearing a thematic relation to immediately preceding difficulties or frustrations arising from the life situation. Thus a woman of 59, a second concubine who had been widowed, who had lost her only adopted child and whose future promised much loneliness, became possessed by her dead husband and her cousin; at various times she nursed a pillow as though it was her departed child and kept talking frequently about coitus. Other cases acted out dramatically the imagined behaviour of the possessing personality, but revealed "double orientation". A widow of 47, for example, who was an ex-cook at the time working in a temple, lonely and isolated in Hong Kong, became possessed by the Goddess Kuan-yin, or the Goddess of Mercy, comparable in several respects to the Virgin Mary. The patient jumped into a pool saying that the Goddess was taking her bath, but also said that she, the patient herself, was washing away her bad luck; she poured water over her head and said that she was feeding the Goddess. Out of the total 66 cases, 36 showed reasonably clear thematic content in their symptomatology. Twenty-eight of these were women, there being no significant difference in the proportion of these thematic cases in each sex. As might be expected, organic cases did not show systematized trends and provided only a caricature of possession.

Mood was congruous with content in 2 cases of depression, and one of these had attempted suicide. Two cases were ecstatic, seeing the doors of Heaven open before them; one of these was a manic case, the other a hysteric. Two

females had experiences of coitus with the possessing spirit, one a departed relative and the other a living clairvoyant she knew. The so-called gift of tongues was shown by 2 Christian patients who spoke, or rather gibbered, in what purported to be Hebrew and English. Two other patients spoke allegedly with the voices of the Goddess of Mercy and Jesus Christ, a third with the voice of a strange man and a fourth with that of a five-year-old child. One patient declared that the Goddess of Mercy only possessed the upper part of her body since the lower part was unclean due to her having been a prostitute before. One woman burst into a cold sweat with a rapid pulse, a second complained of heat, and a third felt that she had suddenly become old, with white hair. There was one peasant woman, an hysteric, who declared that an evil ghost was clutching at her heart and stopping it; on examination it was found that her pulse had actually weakened, but she was practising Valsalva's manoeuvre, i.e. closing her glottis and forcibly increasing her intra-thoracic pressure. One schizophrenic girl said that her possession started after she had been staring at the Virgin Mary; she felt her body becoming only skin and bones, whereupon the Saint entered her.

Apart from the female epileptic patient who became possessed after a series of epileptic fits, 1 male and 1 female hysteric had thrown hysterical fits in the past.

PRECIPITATING CAUSES

Organic precipitating causes were phthisis (in 3 cases), cholecystectomy (1), epileptic fits (1), amphetamine intoxication (1, also included among the above 3 phthisis cases), lactation (1), insulin hypoglycaemia (1), and a febrile illness, probably influenza (1). Still another case, diagnosed hysteria, had had a fever a few days before the abnormal behaviour developed. Both the last 2 cases also had been subjected to psychological frustrations.

Cases with definite psychological precipitating causes were also those showing thematic content in their symptoms, and these have already been mentioned above. In 4 of these the conflict arose from the existence of concubines or from extra-marital liaisons of the husbands. Four female cases were married for the second time (there is a tendency to frown upon the remarriage of women, especially in the case of widows.) Two cases were troubled by religious conflict; one, a young woman, was possessed by the Christian God after she had been subjected to intensive proselytization by a fundamentalist sect while a patient in a tuberculosis hospital (see case history below); and the other, a peasant woman, possessed both by Christ and a Taoist God, had developed guilt over her failure to tend to the memory of her dead husband in traditional ways after she had come to Hong Kong and obtained help from a Catholic group for herself and her child. One male case developed possession by his father's spirit after he had repeatedly dreamt about the latter reproving him for not reverencing him.

Several of the illiterate female patients were superstitious, believing in fortune-telling and the quasi-Taoist spiritualistic cult. When asked a leading question two of them admitted that they had thought of becoming professional mediums themselves. Three cases, all female, dated their possession or their preoccupation with possession from the Taoist-Buddhist equivalent of All Souls' Day (when the dead are supposed to return to earth).

TREATMENT, OUTCOME AND FOLLOW-UP

Treatment was for the basic illness. Eleven out of the 16 schizophrenics were given insulin or electroplexy, or both. All 33 hysterical cases, with the exception of 7 who recovered with psycho-therapy, were given electroplexy, the courses averaging 7 shocks only. All in our series were discharged with their illness fully remitted except 7 cases who were only partially remitted. These 7 comprised 5 schizophrenics, 1 case of G.P.I. and 1 senile dement.

A follow-up study was made in October-November, 1958, i.e., nearly 2 to nearly 5 years after the discharge of various cases. A letter was sent out asking patients to come for re-examination, or if that was impossible, a detailed report on their present condition was requested. The results are set out in Table IX. The criteria for considering a patient as "well" were freedom from symptoms and ability to continue with their usual work.

TABLE IX
Results of Follow-Up

	Well	Unwell	Total
Letters returned by Post Office			8
No reply			17
Patients interviewed	22	1	23
Patients whose relatives were interviewed ..	2	2	4
Re-admitted and discharged	3	1	4
Re-admitted and still in	—	1	1
Information by letter	6	3	9
	33	8	66

TABLE X
Results of Follow-Up, by Diagnosis

Diagnosis	Total with Known Outcome	Well	Unwell
Hysteria	20	20	—
Schizophrenia	16	10	6
Depression	3	3	—
Post-epileptic confusion	1	—	1
General paresis	1	—	1
	41	33	8

Out of 41 cases (8 males and 33 females) about whom information, mostly direct, was available, 33 were found to be well (6 males and 27 females). Table X gives the results in terms of diagnostic categories. The poor outcome of organic and schizophrenic cases is not surprising. It should be noted that one female case of hysteria and one female case of depression with hysterical features, although well at the time, had been re-admitted, and discharged shortly before the follow-up study. The first of these was a phthisical concubine and prostitute who had deserted her husband, in conflict with the man she was living with because, although he could not give her sufficient money, he refused to allow her to go out to work. The second had at first been admitted as a case of manic excitement and had then come in again basically with depression and

insomnia; she was an immature and demonstrative type of person, living in much poverty and in constant conflict with her neighbours. Only the first woman manifested possession on re-admission. It is important to note that none of the cases found still unwell, including the one remaining in hospital, continued to show possession symptoms. (Two admitted that they were sometimes troubled by dreams of dead relatives communicating with them.) This suggests that the possession syndrome was not an intrinsic part of the illness, in organic and schizophrenic cases, but only a hysterical overlay. All but one of those directly interviewed said on being asked that they no longer believed in the possibility of possession, although this may be doubted. One young schizophrenic girl still thought that the Virgin Mary could possess people in order to help them.

PROGNOSTIC FEATURES

Sociological factors like education and class possibly had an influence on the readiness with which replies were made to our letters in the follow-up, so that care is needed in assessing the significance of the characteristics of those 41 cases whose outcome was known. Subject to this proviso, there was not found any significant difference in either the educational or the class levels of the 33 fully remitted cases when compared with the total material in the present series. Nor was there any such difference as regards sex, age of onset, civil status, or degree of possession. Furthermore, there was no evidence that the presence of thematic content led to a better outcome, a fact surprising at first sight. If we took only the 23 fully remitted cases diagnosed hysteria or depression with hysterical features, i.e., cases which might be expected to be wholly psychogenic, and compared them with our total series, there is still nothing of prognostic significance that emerges.

The following general conclusions may be drawn: Hysterical cases of this syndrome have an excellent prognosis, whether or not precipitating causes are obvious; but a poor outcome will be associated with a difficult life situation, as illustrated by the case of the phthisical concubine mentioned above. The prognostic significance of thematic content depends therefore on the actual nature of the life situation inducing the possession, and whether alleviation of this is possible. Much the same may be said of cases of depression (with hysterical features). The prognosis for cases with other diagnoses is in general that for the under-lying illness, but I have the impression that possibly schizophrenia presenting with this syndrome tends to have a relatively good outcome; the diagnosis from hysteria of these cases may of course be difficult.

Lhermitte, as mentioned above, believes that cases with an insidious onset and gradual evolution, showing lucidity and an absence of clouding of consciousness, have a poor prognosis. Comparison of the present case material with those described by Lhermitte and other French authors must naturally be cautious, since the latter cases may have been selected for psychopathological interest, and also the factor of management and treatment needs to be controlled. But I can say that with experience of many thousands of Hong Kong patients I have never seen a case of the kind that Lhermitte regards as lucid and insidious, and predestined to chronicity. Moreover, most of my cases were poorly educated or uneducated, and many of them women plunged into states of clouded consciousness through meeting real and serious environmental difficulties; while the French Catholic cases of demonopathy described in the recent literature were as often as not men rather than women, few of whom

could have been without formal schooling. Many of these latter cases appeared to have deep psychological conflicts of a moral kind, e.g. often over homosexuality; and highly structured psychoneuroses like obsessional states are described as underlying the syndrome. I have not seen a single obsessional Hong Kong patient presenting with possession symptoms (although obsessional states are otherwise encountered). Most of my cases were, on the contrary, cases of pseudo-psychotic hysteria with more or less clear thematic content in the symptomatology, or similar cases of depression with hysterical features, many of them understandably precipitated by frustrations and deprivations, and of good outcome. Moral conflict over sexuality in Hong Kong patients apparently takes other forms than possession, and homosexual conflicts are rare.

From a strictly scientific point of view, these differences may be ascribed to the contrasting cultural, or rather religious, backgrounds of the Catholic and our Hong Kong patients. Whereas Catholics believe in the reality of Satan as *the source* of all Evil, prone to obsess and possess them, the Chinese have not a similar "personified" concept of Evil with which they may associate in mythopoeic thinking their moral lapses. This is discussed below in some detail. Belief in Satan has a powerful psychological effect and imports the notion of possession by him into serious psychological conflicts (which necessarily have a moral aspect), leading perhaps to chronic psychoneurosis. In the Chinese, however, this particular syndrome is more often of a reactive and situational kind, if uncomplicated by other illness, clearing up with improvement in the patient's circumstances. It should be noted that while most of the French cases are those of demonopathy, there are also instances, the frequency of which is not clear, of possession not by Satan but by succubi, incubi and animal familiars. These latter kind of cases are probably closer to those that are seen in Hong Kong. The distinctions made above are no doubt of suggestive value only, for they are posited on the assumption that the cases in the French literature of recent years are representative ones. To analyse a series of French cases in a way comparable with what we have done with our material would be of the greatest value*.

DEFINITION AND FORMULATION

It will be helpful to introduce discussion of the psychopathological aspects of possession with a definition of the condition. This definition makes use of Mead's analysis of the Self into the "I" and the "Me": Possession is a condition where problem-solving processes result in an unusual dramatization of a certain part of the "Me" aspect of the Self, that part being constituted by forced and urgent identification with another personality, believed to be of transcendental nature, whose relationship to the subject is not tested in reality but is elaborated in fantasy. The nature of the possessing personality can be psychologically understood in the light of the subject's own personality needs; his life-situation; the personality characteristics, either historical or symbolical, of the possessing agent; and the subject's cultural background, which determines the normality or otherwise of such a condition.

For possession to occur, all the following factors will be necessary, though

* Dr. Heinz E. Lehmann of the Verdun Protestant Hospital, Montreal, informs me that in a series of 5 French-Canadian cases studied by him, 3 were male and 2 female; 3 were schizophrenic, 1 hysterical and 1 mentally deficient. Two of these cases were precipitated by involvement in seances. These findings are suggestive and would seem to contrast with ours as regards male preponderance and the infrequency of hysteria, but they appear to be in accord with reports in the French literature.

each may be of different weight: the subject must be dependent and conforming in character, probably occupying a position in society that does not allow her (or him) reasonable self-assertion. The subject must be confronted with a problem which she sees no hope of solving, the problem arising from personal needs either of an instinctual kind or else concerned with her self-esteem. The existence of folk-beliefs in possession, shared with other members of her culture or sub-culture, enables the patient to achieve an unrealistic solution of her problem by internalizing a possessing agent with characteristics appropriate for the solution of the conflict. This form of transitory escape from reality is facilitated not only by the urgency of the patient's emotional needs in relation to the possibilities for meeting them, but also by the existence of organic or toxic factors which enhance mental clouding and fantasy thinking.

DISCUSSION OF PSYCHOPATHOLOGY

I find it difficult to agree with Lhermitte (1944) that possession is not a legitimate syndrome. In discussing this point it is appropriate to confine ourselves to the complete syndrome occurring in pure culture on the basis of a pseudo-psychotic hysterical reaction, and disregard the fact that elements of it may indeed merely be a picturesque coloration given to other illnesses. That possession is hysterical in basis is evident from the manifest characteristics and natural history of the great majority of pure cases of possession, whether these are regarded as pathological or not. The pure form of it has no nosological independence, but it is a unique disorder of the Self (conceived psychologically and not metaphysically), a disturbance in the balance of what Mead calls the "I" and the "Me"; and as such it possesses a considerable degree of coherence. For this reason it can be justifiably regarded as a syndrome.

There are two established approaches to the study of our subject, and they are not mutually exclusive. The first, which invokes the concept of hysterical dissociation and mental automatism, is the classical line of research initiated by French psychologists and psychiatrists. Little need be said about this except to point out certain aspects of thought in this field that are not usually emphasized*. There is the welling up during hysterical delirium of "mythopoeic thinking", a term more apposite and meaningful in our present context than the allied "dereistic" or "catathymic" thinking of E. Bleuler and H. W. Maier. E. Cassirer (1944) has stressed the fundamental importance for the human mind of "mythopoeic" thinking. It is possible that this kind of thinking can help the individual to grasp a profoundly complex life-situation, as a first step towards further action and self-development. The French concept of *mythomanie*, which is a type of hysterical puerilism, is one which deserves wider recognition. A myth has been defined as a proverb in story form, and mythopoeic thinking has in fact more thematic content than dereistic and is less directly complex-determined than catathymic thinking. Furthermore, mythopoeic thinking is associated with congruous affects, and may be accompanied

* It is appropriate also to mention here R. W. Thouless' review (1937) of Whately Carrington's experimental research into the mediumistic experiences of Mrs. Osborne, making use of association tests. Thouless concluded that there was evidence of the possibility of secondary personalities formed by processes of repression. Gardner Murphy has published two critical surveys (1953, 1956) in this field, the first of which attempts to evaluate the present status of the "dissociation theory". A. Z. Orzeck *et al.* (1958) have recently tried to demonstrate the production of different personality organizations in subjects given hypnotic suggestion. Two papers of medical and psychological interest in the *Proceedings of the Fourth Conference of Parapsychological Studies*, New York, 1957, are disappointing but may be mentioned for the sake of completeness: A. Assailly, "Some characteristics of mediumship", p. 69 f.; and C. A. Meier, "The Psychological Background", p. 104 f.

by hallucinations which Clérambault (see discussion appended to the paper by Leroy and C. Portier, 1930) has called "sensory echoing of ideas" following what he regards as a total state of sensitization of the psycho-sensory apparatus. It is the thematic coherence found in mythopoeic thinking that in such cases provides a nexus for the organization of an accessory mythical personality manifesting itself in actual behaviour.

A second and less familiar approach to the study of possession is that of Jung, and this supplies a more clearly organismic and prospective point of view to supplement that mentioned previously. As early as 1902 Jung stated that the possessing personality, occurring typically as he thought in adolescents, was a personality idealized in the mind of the subject, and one struggling to be born, i.e., to actualize itself in the behaviour of the latter. Somnambulistic states he considered to be teleological in basis, since they were the means whereby the future personality could temporarily express itself. In 1921 Jung made an interesting formulation that opens the way for research in the wider context of comparative psychiatry. He distinguished on the one hand complexes split from the personal unconscious, and on the other those arising in the collective unconscious; to the former he referred the idea of the "soul" and to the latter the idea of "ghosts" or "spirits". There is thus the possibility of classifying possession states into two kinds which may be of psychological significance: those involving possession by departed relatives, and those by culture heroes, deities, daemons and Satan.

Considerable spade-work has still to be done in this area, but it may be noted that already there exists a heuristically useful common point of departure for the study of the *psychology* of eastern and western religions; Jung, along with his penetrating studies of the latter, has also acknowledged (1957) the common denominator between his system and the Buddhist theory of mind. D. T. Suzuki (1949) has pointed out that the psycho-analytic Unconscious coincides with the superficial layers of the Buddhist conception of Mind—layers containing fantasied figures of gods and daemons which may or may not be projected (see also R. Wilhelm, 1942).

The Jungian point of view is more helpful to us in our attempt to understand the origin and growth of the possessing personality than the mechanistic analysis of those who employ the concept of mental dissociation. However, Jung's explanation of the development of subsidiary personalities emphasizes the spontaneous evolution of complexes in the unconscious with scant reference to the external circumstances of his subjects; and the associationists have little to say on this point except in so far as they have adopted Freudian explanations which invoke the sublimation and reaction-formation of instincts in general character development, the Freudian Ego being conceived simply as an executive agent without any attributes. The crucial question can still be fairly posed, why and how a certain personality appears and not another, and how this personality is related to the social setting in which the subject finds herself.

We may turn to G. H. Mead (1934) and H. S. Sullivan (1953) for certain suggestions. According to the former, the Self is a "social process" in two phases, each one reacting on the other; there is the "I" or Ego with its conative tendencies, and there is the "Me" consisting of the organized attitudes of others which we have assumed ourselves and which influence our self-conscious conduct.

Now my hypothesis is that possession involves the pathological or at least the unusual predominance, temporarily, of one phase of the Self at the expense of the other; of a certain portion of the "Me" at the expense of the "I", this

part of the "Me" having developed from the internalization (but incomplete assimilation) into the subject of personality traits derived from either the known personalities of departed relatives or those of culture heroes, deities and daemons. Here it should be pointed out that most possessed subjects, if asked to tell carefully who they are, will reply that they are still themselves, but that the possessing agent is speaking through their mouths; a few may say, however, that they are the possessing agent, but are making use of the body of the patient. In other words the majority of cases still preserve the original identity of the "I" even though the "Me" has been split from it by organization round a particular alien personality. In extreme examples this personality becomes so active that not only does it dominate the "Me", but there is a phase reversal of "Me" into "I" and vice versa, although the distinction between the two is always there to be made introspectively by the subject.

This schematization of the two phases of the Self is also to be found underlying Sullivan's thinking. One of his central ideas is the formation of the Self through the assimilation of other people's appraisals of the subject into the latter's "Me"; although Sullivan emphasizes, whereas Mead does not, the genesis of the self-system from anxiety. Sullivan has stressed the importance in the development of the Self of the capacity for taking the part of others, or role playing. Every child has the natural tendency to dramatize his strivings by taking the role of another person, to act in the way he imagines this person would act. At first this person would be a parent, but later it could be someone else, whose personality and status characteristics enable the subject to evade tension and punishment or obtain approval. Each role tends to be organized around a certain personality, but it will not correspond to an exact copy of that personality, since various dynamic trends in the subject will distort it. Thus different sub-personifications of the Self arise.

The above analysis of the development of the Self may be illuminated by discussing it in terms of the assimilation of moral values by the subject. Personality can be usefully looked upon as an organization of values which are consistent with one another (P. Lecky, 1956 and A. Wheelis, 1958). A personality is the bearer of values, clear-cut and fundamental ones in the case of institutionalized personalities or figures, and less important and universal ones in the case of individual persons, whether living or dead. The assumption of roles centred on other personalities is essentially the assimilation into the Self of new values inherent in those roles. The normal personality is naturally resistant to the penetration of new values that are not in keeping with the subject's valuation of himself, i.e., of his value-system. The new values are either rejected, or the personality has to undergo a re-organization in order to preserve its unity. We may say also that the new sub-personification will be either kept dissociated from full awareness, or else will be fused into the conscious Self, to bring about in it a transformation.

Now re-organization, if gradual, need not lead to pathological manifestations. But if new and very different values have to be acquired by a subject in order to meet a crucial and radically novel situation, always with the need to avoid or reduce tension and maintain self-esteem, there may not be time for gradual adjustment. Then it is possible that a certain sub-personification appropriate to the demands of the situation may come to assert itself and gain overall domination of the subject's behaviour. This would be a state of possession by another personality. Normally this would more easily occur in the young, since the integrative tendency associated with maturation is in them weak. In abnormal individuals it would occur more commonly in those who

are immature, and for such persons this process will be one method of adaptation to environmental demands.

Until now I have dealt only with those cases of possession where personalities bearing desirable values are manifested, personalities such as those of deities, culture heroes or other individuals of respected status in the eyes of the subject. Most possessing personalities have a positive or negative moral relationship to the value system of the subjects, although those which are the spirits of departed persons may be difficult to assess in these terms. Are we able to suggest an explanation for the manifestation of morally negative possessing agents like Satan, minor fallen angels, mischievous, revengeful ghosts, and the like?

The assumption of roles identified with other personalities is only one mode of reaction to disapproval and anxiety-provoking situations. The other mode is a dissociation of certain components of the personality and their loss of representation in awareness because they are censured by significant persons in the situation. This can take place with varying degrees of intensity, depending on the anxiety aroused. Even though these components are dissociated they can still be moulded and organized into a dynamic part-system by the forces that have brought about their dissociation from the rest of the self-system. It will not be surprising if they, being the product of unacceptable tendencies from within, become embodied or personified as symbolically evil figures. To the extent that they are rejected they can be released only with difficulty in markedly abnormal circumstances, e.g., in deeply rooted conditions like an obsessional psychoneurosis rather than a superficial twilight state or delirium. In so far as they are fully dissociated and unconscious they are also bound to be difficult to re-integrate, and in keeping with this, the abnormal conditions amidst which they appear will be the harder to rectify.

This dissociated system represents the rejected anti-social tendencies of the subject and forms that part of the personality which Sullivan has called "not-me" (Cp. Jung's concept of the *persona*, and its conflict with what is the true Self. This idea is also to be found in Sullivan, 1953, p. 209). Under certain pathological conditions these tendencies well up into awareness accompanied by dread feelings of extreme anxiety. In this process personification naturally occurs since the subject is thereby enabled to ascribe the undesirable aspects of his own personality to other persons, or other creatures not related to himself (Cp. the Jungian concept of the *shadow*. As for the Devil personification, Jung would maintain that this exists as such in the Unconscious but is projected on to the cultural environment when it is not fully understood and recognized. See *The Secret of the Golden Flower*, p. 112). For Catholics the figure of Satan is, psychologically speaking, always at hand to help elicit and make manifest this process of personification. Conditions which manifest possession by the Devil—the source of fundamental Evil—are thus according to my hypothesis comparatively serious ones, since they involve the release of material deeply buried in the "not-me" part of the Self. While the use of sub-personifications as an aid in adapting to urgent environmental demands is easy to understand when they bear positive values, the emergence of the Devil personification is more difficult to explain directly in terms of environmental or situational factors. It suffices to note that such a personification appears mostly to occur in severe pathological conditions like obsessional-compulsive states. But it is possible nonetheless that certain cases placed in particular circumstances may obtain secondary gain at a superficial level from the projection of blame on to the Devil or to subsidiary fallen angels or vengeful ghosts; for the demonstrative

disavowal of guilt before the eyes of significant persons is likely to result in the reduction of anxiety.

Clearly, the situation in which the subject finds herself, the circumstances surrounding the process of possession, are all-important. There must be present an expectant, credulous and receptive audience. Possession is a phenomenon which inspires among those who believe in it mutually shared feelings of awe and perhaps reverence. The god-possessed individual gains as a rule an elevation of status, and the devil-possessed attains a position which produces in others fear, a suspension of criticism, and a posture of retreat. How important the attitude of the group can be as a factor in maintaining the phenomenon is well illustrated by the Scottish case described by R. W. Pickford (1943) of a woman whose powers of mediumship rapidly waned when she was no longer believed in. One may go further even, and distinguish in particular cases gains of a more specific kind that come from the solution, to the patient's satisfaction, of certain pressing problems confronting herself. Such a solution may only be a fantasied one, made possible by the temporary acquisition of a special set of values inherent in the personality of the possessing agent, values that give new and specific advantage to the subject in trying to cope with the situation. Nevertheless, even fantasied solutions are capable of discharging tension.

In truth, the formula of wish-fulfilment occurring in fantasy (as in dreams) is over-simplified, for wish-fulfilment is only one aspect of what is really a complex teleological process. It is never a question simply of fulfilling a wish, but the apparent fulfilment is only one attempt out of several to define clearly and grasp certain problems in order that the subject might be the better able to solve them. The "acting out" more or less directly of fantasies must similarly be regarded as an intermediate step towards reasoned, discriminative and consciously purposeful action aimed at solving the conflict that has given rise to the fantasies in the first place. This then is the meaning of the process of *dramatization* which is so evident in possession. It is an expression of adaptive, problem-solving behaviour ranging from the acting out of a "wish-fulfilment", through an experimental, probing type of conduct with varying degrees of abreactive satisfaction, to the direct manipulation of other persons involved in the subject's personal problems. It may be expected that patients will exhibit clouding of consciousness of different degrees, varying from a deep hysterical fugue (or delirium or twilight-state), to pseudologia phantastica, and then to malinger and deception without ultimately any clouding at all*. Thus different levels of volition may be involved, and this can be true even of mediumistic cases occurring in a cultural setting that gives support to mediumship (see Herskovits, 1958).

The teleological point of view which we have developed above has recently also been adopted by W. Mischel and F. Mischel (1958) in their attempt to apply learning theory to the interpretation of possession. They suggest that this condition provides an approved model for explaining disturbing phenomena, gives freedom from responsibility for having to tackle immediate problems, enhances self-importance, and also makes possible the control of others. These points are well taken, and they indicate clearly the complex motivation

* As far as Chinese cases are concerned, the common appearance of culture heroes and deities as *dramatis personae* in the popular opera must have a powerful effect of the imagination of ordinary people. It is interesting to note that the door through which actors enter the stage is conventionally called the "Ghost Door", and there exist legends about actors being possessed by the spirits of the characters they impersonate. I am informed by Dr. G. S. Philippopoulos that possession by gods and goddesses of the classical pantheon occurs in Greece, much as they were presented in ancient myth and drama.

behind the possession process as well as the rewards that lead to the stamping-in with repetition of this unique kind of behaviour. One must be cautious, however, in trying to explain cases involving possession ideas on a teleological basis. The notion of possession may come into the content of the symptomatology at a superficial level, just like any other ideas derived from the subject's cultural milieu, and there may be little of psychopathological significance in it.

CASE STUDIES

The foregoing discussion of psychopathology can be illustrated by a number of selected case histories. It has been possible to distinguish three basic motivations underlying the symptomatology of our cases. *First*, the dramatization of fantasied attempts at wish-fulfilment; *second*, the dramatization and working through of guilt conflicts; and *third*, the manipulation of surrounding persons. The first kind of case appears to be the most, and the third the least common, but the majority of patients demonstrate mixed motivation so that in many the interpretation of symptoms is by no means easy. This of course is true especially of those cases which are basically schizophrenic or organic. So-called "pure" examples of the syndrome would consist essentially of the first kind of case.

I. *Dramatization of Fantasied Attempts at Wish-fulfilment*

A woman of 45, married to a railway worker and with five children, had come down to Hong Kong by herself. For 4 years she had been treated in a tuberculosis hospital. She had had only about 5 years' schooling and had before marriage worked in a kindergarten. Two of her sisters had died of phthisis in their youth. For a number of years she had been troubled by a dream, during which she would find herself in a room with one of her dead sisters, each lying on a bed, and the sister would pull her over, whereupon she would wake up in a fright. She was by personality a meek and trusting woman, of average intelligence.

She had been in contact with Christian Chinese for some years and had been interested in the Congregational Church, and later in the Anglican Church, but she was never baptized. Latterly she had been greatly influenced by evangelists of the Assembly of God, both Chinese and western. This revivalistic sect believed firmly in the possibility of possession by God and the cure through this means of various illnesses. The patient was suffering from chronic pulmonary tuberculosis with cavitation and had recently been advised to have a thoracoplasty operation done. She was rather troubled by this and was made all the more uneasy by the fact that the evangelists visiting the hospital had told her that she was sinful and that if she believed in God she would be saved; the Holy Ghost would possess her and thereby cure her without the need for an operation at all.

While normally she appeared to have made up her mind and would press for her transfer to a general hospital for the operation, she at other times became confused and would not consider it at all. She wandered about during these episodes, mostly at night, sometimes appeared to pray, and at odd times said that she was taking on herself the task of driving away devils from the other patients. She said that she could see God when she had her eyes closed. This continued for several days and then she became lucid again. However, after a further 10 days she became mute and tearful at different times and started to speak in what purported to be English and Hebrew. She declared that she was possessed by two different Gods. One of these was Jesus Christ and when possessed she declared that the patient was to follow Him, that He would return among men, and that she was to be well and have eternal life. The other God was obscure in nature, but told her and her audience in a mixture apparently of English and Hebrew (which she later "interpreted") that she should be a prophetess to help remove pain and sorrow from all the world. She was then admitted into the mental hospital and made an uneventful recovery after two weeks with sedation and psychotherapy.

II. *Dramatization and Working Through of Guilt Conflicts*

A woman of 27, illiterate and of peasant origin, was admitted because she had been possessed by the spirits of her dead husband and mother. She had been widowed 2 years previously, her husband, a farmer, having died of typhoid. She had 2 young children with her; 1 infant had been given away earlier because the family was too poor to support it. She did odd jobs as a casual coolie and also hawked vegetables. She had received help from a religious welfare organization and had for more than a year become a Catholic.

Her early history was of great interest. At birth she was given to her eldest uncle, because they were childless and it was important for the eldest son to have children to carry on the rites of ancestor reverence. She called her own father "No. 5 papa". Later she was again given

away as a child-bride to another family, and as was the custom for her part of the country she grew up with her future husband and formally married him at the age of 16. She was poorly treated both by her parents-in-law and by her husband.

She was an unintelligent, conforming and superstitious woman, overwhelmed by the task of bringing up her two children in the difficult city environment. She was unhappy over her decision to change her religion; and over the fact that since her husband's death she had not been to tend his grave (she did not know the way to get there and moreover had no money to do so). Her neighbours had been criticizing her for her change of faith. Furthermore, a fellow worker had proposed to her, but she was reluctant to accept the proposal because it was considered immoral for a widow to re-marry. Finally, the last straw was her being cheated of her salary about 6 days prior to admission.

She cried, became agitated and sleepless, and expressed the fear that her children would be taken from her and that she might be forced into a second marriage. She had dreams of meeting her dead relatives in Hell, of being reproved by them for neglecting their graves and changing her religion. She thought she heard people saying that she was over-sexed and that they would persecute her family. Then she related that her husband had had intercourse with her, night after night, and she was not sure that it was only in a dream. Her husband also possessed her and spoke, through her own mouth to her apparently, saying that it was fortunate that her friends had advised her against re-marriage or else she would have succumbed to the temptation. He also told her that he did not like Christianity, and threatened to bring her down to Hell. At other times her mother possessed her and said that although she similarly disliked her change of faith the husband should not bring her to Hell. The patient became rather depressed and full of guilt, sighed and beat her breast, saying that there was no way out for her, since whatever she did would offend either the Virgin Mary or her own gods. Later she made two suicidal attempts.

She was diagnosed as a case of hysteria, and recovered after 4 months with a course of E.C.T. On follow-up she was well and free from possession although still mildly troubled and depressed because of her difficult conditions.

III. *Manipulation of Surrounding Persons*

An illiterate and ignorant woman of 36, married to a salesman, was admitted because she manifested symptoms of possession by her dead infant and a deity. She had two young children, and the infant had died more than a year previously, aged 4 months.

Her early history again revealed that she may have had difficulty in developing stable identifications. Born in a peasant family, she was adopted by a family who did not treat her well, and because of her complaints against the other children of the house, was given to another family, who was kinder to her. Later she was inveigled into coming to Hong Kong by the promise of a job as maid-servant, but was drawn into prostitution instead.

By personality she was light-hearted, friendly, submissive, immature and superstitious. She was known to be in the habit of exaggerating her minor discomforts and illnesses like a cold. Her husband had become unemployed some months previously, and had had to borrow money to become a hawker, or pedlar. She herself had been gambling in secret, and unknown to her husband had lost a sum of money she had borrowed. She lived in a rent-free house which the landlord wanted to repair, and it was intended that after this had been done rent would be charged. The patient strenuously objected to the repairs, and when these were later effected she moved out. About the time that the repairs were being carried out her infant died and she was resentful that the inconvenience she had thus been put to was responsible, as she believed, for her inability to save the infant's life. When her baby died she had been confused for a day, scolding incoherently the principal tenant, and reported seeing ghosts.

About three weeks before admission, just before the anniversary of her son's death, she dreamt about him one night, and according to her account, he told her that he had died because of the principal tenant's actions in repairing the house, and wanted the latter to make amends. At this time she had already moved back to the original house at the insistence of the husband, who feared that she was becoming involved in an affair with a man living in the house to which they had temporarily moved. She became confused, lost her appetite and started to pray, even on the streets. Then she became possessed by an apparently Taoist god, although she showed no change in demeanour when this occurred. The god next brought on her infant's spirit, and she started to cry like a baby, and also talked in a babbling way with associated childish mannerisms. Before and after the possession she nodded violently and this happened several times a day. She said when possessed that he, the infant, had been murdered by the principal tenant, that he was unhappy in the other world and wanted recompense. She also scolded other people around during such periods. However, neither her husband nor her neighbours including the principal tenant believed her and her husband went so far as to slap her.

She recovered after superficial psychotherapy in hospital and was discharged in 5 weeks.

THE CULTURAL BACKGROUND

There is no essential psychological difference between spirit-mediumship as practised in Hong Kong by certain local cults and the possession phenomena

seen in cases sent to hospital; nor is there any between mediumistic phenomena in Hong Kong and that in the West. The similarity in the latter case is in one respect striking. Many western mediums need to contact a Control before they can bring up a departed person's spirit, and the same is true of mediums in Hong Kong who first have to contact a deity. This parallelism is likely to be due to an underlying psychological mechanism common to both, rather than to culture diffusion. (Jung makes the point that mediumistic Controls are often of the opposite sex, and attempts to relate the Control to the *anima*. See *The Secret of the Golden Flower*, pp. 115-116, 117.) The Control is usually a person of repute in the medium's eyes, and so of course is a deity; and both have numinous prestige. It is possible that dissociated systems centring on such personalities have become liberated with ease by practice, the process beginning with the medium ritually concentrating all her attention on to the Control or deity to produce a monoideic state. Once these personalities have emerged other processes of dissociation can then take place to allow the release of subsidiary personalities. B. Harper (1957) has described how in Mysore possession is also preceded by lengthy worship of a deity.

Spiritualist cults in Hong Kong have a wider following than in the West. There is not, however, an attitude which regards possession by a deity as the supreme religious experience, such as one finds in Afro-Caribbean culture. (See M. J. Herskovits, 1951, p. 66; also L. Mars and G. Devereux, 1951, and M. S. Wolff, 1956.) In Hong Kong there is no "worship" of deities manifesting themselves in the persons of mediums, but a significant number of illiterate women and a very few men believe in consulting oracles for knowledge and decisions of a supernatural kind, the mediums mostly being ensconced in vulgar Taoist-Buddhist shrines or in their own tenements, where they set up altars and charge fees for the help they affect to give. Many of these are charlatans inasmuch as they merely pretend to be possessed and are not capable of genuine dissociation.

It is necessary to discuss briefly the general background of Chinese religious beliefs, although it is impossible to make any but the broadest generalizations about Chinese culture. We are not dealing here with the culture of, say, Raymond Firth's Tikopia, whose island can be put within London's Hyde Park; and contemporary developments have made the epithet "Chinese" even more confusing than it has been. In the field of Chinese religious and supernatural thought, generally speaking, we need to distinguish customary folk beliefs from Taoist-Buddhist religious doctrine on the one hand, and serious Confucian-Buddhist-Taoist philosophical speculation on the other. Folk or peasant religion grades into commercialized spiritualist cults like those we have already mentioned, and also into folk-lore and mythology. Here we encounter the equivalent of the Western vampire belief, i.e., the belief in malevolent ghosts, the survival of persons who have died violent and unnatural deaths—although the vampire as such is not known (Cp. also the Roman *larvae*). There is too the folk-belief that the ghosts of foreigners or those of people who have no descendants to reverence (or "worship") them may be "unsatisfied", become *revenants*, and seek to return among the living by possessing them.

The popular Chinese attitude to the spirits of the departed is a complex one. Not all ghosts are feared in the way mentioned above. Some are even welcomed, as evidenced by many folk-tales (Cp. the Roman *lares*). This brings us to the question of Confucian ancestor reverence, often miscalled "ancestor worship". In the Confucian Canonical books there is mention of spiritual beings, including the spirits of those who have died, but nothing about

possession. It is taught that departed relatives should be revered ("sacrificed to") with the same *propriety* that filial piety would have accorded to them when they were alive; and also that to reverence ancestors not one's own is mere flattery. It is not a question of sacrifice or a peace-offering so much as a thanksgiving and particularly a communion feast, inasmuch as the "sacrificial" food is later distributed among different members of the family. Even E. B. Tylor (1891) did not insist that all "ancestor worship" was propitiation of the dead. Confucian ancestor reverence therefore springs from love and not from fear, and a family will pray for the well-being of their ancestors, much as Catholics will pray for their dead who are in purgatory. This practice indeed has become generalized in Chinese (Mahayana) Buddhism so that the devout pray for the redemption of all wandering souls, including those of unsatisfied ghosts, to help them achieve the higher planes of transmigration. Such an attitude is not to be confused with the propitiation of unsatisfied ghosts in Hades, a folk practice of the unlearned which merges into the ritual manipulation of deities in superstitious Taoistic rites.

Chinese Buddhism basically teaches that there are enlightened souls or Bodhisattvas who, denying themselves ultimate Buddhahood, tarry behind in order to bring salvation to all living creatures. Among the Bodhisattvas is Kuan Yin, the merciful Madonna, who is believed by many to be able to incarnate herself among the needy and suffering to achieve her noble purpose. Naturally the conviction with which such a belief is held by a person depends on a number of psychological factors.

The above discussion, over-generalized though it has to be, is important for our understanding of the psychology of Hong Kong Chinese in regard to the phenomenon of possession by what might be called transcendental "personalities". One important point that remains is the traditional Chinese concept of the nature of Evil and how it differs from the Christian (or ultimately Babylonian) concept of Satan, the Chief of the devils. Educated Chinese have since early times been disposed to take an agnostic attitude towards the supernatural. They never held the idea of God as a law-giver, jealous and punishing, omniscient and all-good; nor was there the concept of Satan as the source of Evil. The Confucian Canonical Books (c. 500 B.C.) contained only minor references to a vaguely anthropomorphic "Heaven". The *literati* believed that there was a moral order in Nature and that evil resulted from a lack of harmony in the Universe, manifesting itself at different levels, and the problems of evil was continuously debated on what were in fact naturalistic, humanistic and, later, metaphysical grounds*. This ideal image of the agnostic Confucian patriarchy, although impracticably rationalistic for the majority, has been so powerful that to this day men, especially educated men, while taking the leading part in Confucian ceremonies, are often ashamed to worship in Taoist-Buddhist temples and leave these exercises to their womenfolk. This continues to be so among southern Chinese emigrants in Singapore long removed from their homeland; [see A. J. A. Elliot (1955)].

As for the educated Buddhists, they take a mixed psychological and metaphysical view of evil. For them evil arises only from ignorance, desire and hatred and it is inexorably governed by the law of Karma. Some may believe in the

* See P. C. Hsu, 1933; Y. P. Mei, 1951; J. Needham, 1956; and C. K. Yang, 1957. The serious student may consult the study in Chinese by Ch'ien Mu, 1955. H. Benoit (1955) has brought out clearly the contrast between the Buddhist and Christian doctrines of Evil.

The absence of the belief in Satan was of importance for the history of psychiatry in China; see E. V. Zenker (1932).

existence of unsatisfied ghosts and devils in Hell, but these creatures are evil only as a result of moral transgression in a previous life; they are not the source of evil themselves.

We have produced some evidence to show how such cultural attitudes affect the composition of our sample; and how also the absence of the concept of Satan as the source of evil appears to result in a more benign type of the syndrome compared with French Catholic cases. Varying conceptions of the nature of evil and sin have deep psychological, as opposed to moral, consequences, and the role of these in comparative psychiatry is well worth further exploration.

It is also desirable to recognize the importance of socio-economic factors in predisposing subjects to possession. Our analysis has demonstrated some of these very clearly so far as Hong Kong is concerned. It is only recently that the significance of such factors as social class and occupation has been seriously examined in psychiatry, and failure to take social structure into consideration is bound to vitiate comparative psychiatric studies in different cultures, if not wholly invalidate them.

SUMMARY

An analysis is made of 66 Hong Kong Chinese in-patients showing symptoms of possession in varying degree. Characteristics significantly predisposing to possession were: female sex (at all ages), the fact of being divorced, widowed or concubines, illiteracy, and low occupational and social status. Nearly half the cases were hysterical and nearly a quarter schizophrenic. The complete or pure syndrome was infrequently seen and such cases were all female. An attempt was made to identify features of prognostic import on the basis of a follow-up study 2-5 years after discharge.

Many of the patients were (apart from being illiterate and of female sex) suffering from pseudo-psychotic hysteria with understandable thematic content in the symptomatology, or were cases of depression with hysterical features brought on by real environmental difficulties. This appears to be in contrast with data from French cases who not infrequently suffer from more highly structured psychoneuroses based, apparently, on sexual (or homosexual) conflicts. It is tentatively suggested that the difference may be due to the contrasting cultural backgrounds, specifically the belief or absence of belief in possession by a primal satanic figure who is the source of all evil.

A survey is made of contemporary approaches to the psychopathology of possession. A general hypothesis regarding its genesis is offered, illustrated with brief case histories, and a formal definition of the condition is given.

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DRUG-INDUCED SCHIZOPHRENIA*

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INTRODUCTION

MEDICAL research is simpler and generally more productive when it becomes possible to use models. This experimental method is available to psychiatrists who find that certain chemicals called hallucinogens (13) produce in subjects experiences which resemble those described by patients who now have schizophrenia or by those who have recovered. Lewin (19), Kluver (18) and Stockings (31) suggested many years ago that these compounds could be used in this way. However, the differences between these model experiences and schizophrenia rather than their similarities impressed many leading psychiatrists. Thus Bleuler (4) as late as 1956 maintained that lysergic acid diethylamide (LSD-25) produced a toxic delirium and therefore this experience had little to offer to the students of schizophrenia. The fallacy of this argument was discussed by Osmond (23) who with Smythies (24) stressed many points of similarity between schizophrenia and the mescaline experience. The consensus today of research psychiatrists such as Rinkel (26, 27, 28, 29), Hoch (10, 11) and others is that the similarities are adequate, provided generalizations remain within the limits imposed by the data.

LSD produces an experience for many subjects which closely models schizophrenia. There are, however, many differences due to variables such as the presence of insight (the subject has an adequate explanation for the experience being present), the setting, the rapidity of onset, anxiety and the objective. Most schizophrenic patients develop their disease slowly and if they recognize that they are being altered have no adequate explanation. In any event, this alteration leads to an increase in anxiety. When the illness is well advanced anxiety appears to be damped, inappropriate or flat. In fact, some clinicians hesitate to diagnose schizophrenia until this affective deficiency is clearly present. The psychotomimetic drugs, on the contrary, mobilize and deepen the intensity of emotion. The subject may have fear and terror or the euphoria of the transcendental experience, but the affect is rarely flat. In our studies of well over three hundred LSD experiences, we have not seen this. Indeed this intensification of emotion is probably of great therapeutic value in the treatment of psychopathic and alcoholic patients, Smith (30), Chwelos, Blewett, Hoffer and Smith (7).

The reproduction of a model of schizophrenia where a flattening of affect

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is predominant is therefore interesting and may perhaps be useful. This has occurred recently in one of our LSD trials in a normal volunteer and is the subject of this report.

Substances which antagonize the LSD experience are theoretically important, as they may lead to better treatments for schizophrenia. Nicotinic acid, for example, which modifies the experience also cures many early schizophrenic patients when given alone or in combination with E.C.T. (14). Penicillamine is a possible treatment for schizophrenia because *in vitro* this sulfhydryl compound converts adrenochrome predominantly into 5, 6-dihydroxy-*N*-methylindole. The latter is not psychotomimetic (12) whereas the former is (13). Since the psychological activity of LSD-25 is closely correlated with increased levels of adrenochrome in the plasma, it seemed possible that if penicillamine were given with the LSD-25 the experience might be modified because the adrenochrome level would not rise—as it usually does.

PREVIOUS EXPERIENCES WITH LSD-25

The subject had received LSD-25 twice previously under our direction. A partial account of these experiences written by her shortly after follows.

First Experience. The purpose of this experiment was to discover how certain nursing techniques affect someone who has taken LSD-25.

About 15 minutes after the ingestion of LSD-25 (100 μ g.) I became hyperacute to vibration. When the bed was touched very lightly without sound or without my seeing this movement, it felt to me as though the bed were being pushed or kicked. In addition, I felt as though there was pressure behind my eyes and they felt heavy. I had a tingling sensation in my tongue and hands. Within the next ten minutes, I noted a shimmering effect in the room and then patterns starting to form on the walls. When attempting to read, the lines tended to roll upwards toward the top of the page. Forty minutes after taking LSD-25, on looking at my left hand it seemed to shrink and wither. On looking at my feet, they seemed very narrow but as I brought them closer they became very broad and large.

During this period, I experienced some anxiety, irritability and slight euphoria. Some nausea of a butterfly type was noted but it did not remain very long.

During the next two hours, I was subjected to a variety of nursing approaches. When I felt comfortable with the nurse, the room seemed very bright and at times there seemed to be a lovely orange halo around the nurse's head. When I felt rejected and threatened, the room would appear cell-like with very drab colours. On one occasion the nurse assumed the appearance of an animal, then on looking away from her and at my knees, I too seemed to turn into another animal with whiskers growing out of my mouth. This terrified me and I seemed to be wandering around lost in a long tunnel through which the wind was howling. I felt this lasted an eternity when in reality (according to the tape recording) it lasted under a minute. My mood changed quickly but was appropriate to the situation as I experienced it.

The lighting in the room was changing constantly as well as the dimensions. My perception of depth shifted fluidly. Flat surfaces often changed so that I saw what looked like the basic structure of the material. At times a fly which was actually in the room would become a swarm of them in flight. This occurred in the third hour and eventually I came to realize there must be a fly present because a single one would light on an object but none of the others ever did.

My concept of time was disturbed; the day seemed to cover years. My thinking was very concrete and quite paranoid at times. Blocking was apparent during the height of the experience. I was disoriented as to place and person on only one occasion as mentioned above. My emotions were highly responsive. I communicated very little verbally with the observers present—perhaps for two reasons, (1) things changed too rapidly to give a coherent account, and (2) the unpleasant nature of much of the experience.

During the fifth hour the experience receded in waves. It was suggested that I take nicotinic acid 1 gm. by mouth to terminate it more quickly but I refused. I had a tingling sensation over my body and felt the effects of the nicotinic acid would heighten this even more. I was still slightly paranoid on occasion and my mood tended toward mild depression.

From the fifth to the ninth hour I was very quiet and introspective. I was at a friend's home for supper (still under observation) and found it hard to converse with those present. Food was tasteless to me and I was still aware of the "whiskers" in my mouth. I was extremely tired as well. After supper we were listening to a radio commentator, but I was unable to concentrate enough to understand the content. My cigarette tasted odd to me, so at this time I asked to be given nicotinic acid. About 15 minutes after this I became quite alert and felt

normal again. I could follow conversation easily and could now relate my experience to the others.

That night I took Tuinal 400 mg. and slept very well. I awakened in the morning feeling quite refreshed, cheerful and alert. At work that day I began to dictate my recollections of the previous day.

This experience took place four and one half years ago and still remains very vivid in her memory although she referred to her notes for this report.

Second Experience. The subject took LSD-25 to enlarge her understanding of the psychedelic reaction.

About twenty minutes after the ingestion of LSD-25 (100 μ g.) I began to feel slight changes. There was a tingling sensation in my tongue, arm and leg. One half hour after the start of the experience I noted changes in lighting and a shimmering effect in the room.

During this period, music was playing which I found interesting and enjoyable. I felt no anxiety and was quite relaxed, no nausea was present.

Fifty minutes after I took LSD-25, my right hand appeared to change in size and texture. When I looked at reproductions of oil paintings—flowers seemed to be sculptured in clear harsh surfaces. I could see no beauty or life in them. The lighting effect in the room was heightened but there was very little disturbance of depth perception. My mood remained pleasant and I found the experience interesting.

About one and one half hours after the start, I was really into the experience and it remained intense for the next two hours. I was asked to look into a mirror and I saw my image change gradually to that of an older and older "me", until eventually I seemed to get right into the mirror and look out from there. When I looked at paintings of people, they got older, then younger. Occasionally I was completely engulfed in the portrait. I found the paintings fascinating, and landscapes as well were beautiful beyond description, very much alive, and produced a tremendous amount of emotion in me.

When I looked at the people in the room with me, changes occurred in them. One person's face became older, then changed into an Egyptian—later a mosaic pattern formed over his entire face except for one cheek which bore a shield. Sometimes a further change occurred and he resembled a Zulu warrior.

I was able to travel back in time and saw myself at different ages in my family setting and was quite surprised by some events I saw taking place.

I travelled in space to various parts of the world, to other planets and to the bottom of the sea. I found this most interesting and enjoyable. I was tremendously impressed by the comprehensiveness of the universe and the insignificance of the human being with his petty problems.

During these two hours, time had no meaning for me—I was bound by neither time nor space.

Parts of a tape recording of the chanting and drumming by Indians of the Native American Church of Canada performing a peyote ceremony were played for me during the fourth to fifth hour. While I listened, symbolic pictures formed (it made no difference if my eyes were open or closed) by which I felt I could interpret the messages of the drums and the prayers. My emotions corresponded to my interpretation and I was tremendously moved by the whole ceremony.

Time was unimportant to me. I seemed to live a lifetime in seconds. My thinking was very clear. I was never disoriented as to place or person. At no time did I lose sight of the fact that I had taken a drug which had induced this "amazing" experience. I was able to communicate freely to those present what I saw and felt.

During the fifth hour the experience receded in waves. I was somewhat introspective, but at the same time could readily relate to those around me. I felt bathed in a warm glow. I was tired but happy. Music was playing most of the time and I was very responsive to it.

I went to a friend's house for supper and enjoyed the company. I ate only a small meal because I was not really hungry. I told my friends about the experience and we were all very gay.

When I went to bed I took Tuinal 400 mg. and soon fell asleep. In the morning I felt quite refreshed, alert and still retained this feeling of well-being. I had no difficulty carrying out my usual assignments at work during the day.

The subject recalls this reaction essentially as a "feeling experience". The transcendental qualities had a sustained effect upon her.

THE EXPERIMENT

The subject was a female nurse, age 35, who had received 100 micrograms LSD-25 in September, 1954 and again in January, 1958. She had also partici-

pated in many LSD treatment sessions with patients as well as assisting in experiments with volunteers. She was skilful in introspection as well as in verbalization. She was confident in the senior author's opinion that penicillamine given in advance would prevent any LSD-25 experience.

For two days before the LSD-25 experiment, she ingested 2 grams of penicillamine in capsules containing 0.5 grams, in four doses. On Saturday, the first day, she was nauseated after the second dose and thereafter after each dose. During the afternoon she felt lethargic and slept. On Sunday, the second day, she was very disturbed by the powerful odour of the penicillamine which appeared to diffuse from her skin. She remained lethargic and did not sleep well at night. Monday morning, she took a further 0.5 gram capsule at 7.15 a.m. At 9.15 a.m. she was given 100 μ g. LSD-25 by mouth.

Report by Observers

9.15 a.m. She reports the penicillamine odour is making her feel sick.

9.45. She feels some tingling of her hands as well as some numbness. The typical (for her) LSD-25 sensation of something behind her eyes is present.

10.00. The room seems much brighter; objects stand out in sharp detail. Some nausea is present and she is very restless and bothered by the odour.

10.07. She continues to be disturbed by the odour but wonders if she is hypersensitive to it. She now feels cold. Her pupils are not dilated.

10.15. The lights seem dazzling bright. With her eyes closed she can visualize symbols related to the stench. She laughed briefly and appears slightly happier.

10.25. She reports some distortion of depth perception. The walls are either too far or too close. She is very tense and has a marked tremor. She states the experience is horrible but it does not frighten her.

10.40. The subject feels drunk. Mild visual changes are present and she has difficulty in concentrating. Her sensation of taste is gone. Pupil size is 1/4 (pupil diameter one-quarter of corneal diameter).

10.50. Visual changes are very pronounced. Her mood is neutral, then she was able momentarily to enjoy music. Later she visualized a very gruesome-looking object which did not frighten her. Pupil size 1/3.

10.55. Visual distortions are present but not interesting; she is quite indifferent to the visual phenomena.

11.05. She reports she cannot feel emotion. She hears the music, observes the visual changes, smells the penicillamine, but is completely disinterested. When she was asked if she would take more penicillamine replied "I don't care".

11.25. Marked visual changes are present but they are not interesting. The inner tremor is still there. So far the subject has not had any sense of relaxation or pleasure.

11.40. She is visually very alert and can clearly see specks of dust jumping up and down on the revolving record. In reply to a question she denies feeling sleepy. She is not mentally alert, nor tired. Some nausea is present. Now and then she is unaware of her body. Pupils are 1/3.

12.00 noon. She is still unaware of her body but not relaxed. For a moment she felt she was coming out of her experience. She is completely indifferent to music. In response to a query she replied she "could not care less".

12.20. She reports she is definitely coming out of her experience as the

visual imagery is changing less rapidly. The penicillamine odour bothers her once again.

12.35. She feels somewhat more normal and more aware of her body but does not care. She reports she can hear the music but is not interested. Her visual memory is gone. Normally she can visualize people whenever she thinks about them.

12.50. She sees animals in the folds of some window drapery (none are there). The patterns are striking and resemble needle point.

1.05. Visual changes are less noticeable. The room is now stable. Pupils are 1/3.

1.27. She was given one gram nicotinic acid by mouth in order to bring her experience more quickly to an end.

1.42. Visual changes are less noticeable. She is now able to talk more freely. The flush (from the nicotinic acid) starts. She reports little feeling is present.

1.47. She still sees bears and horses in the drapery. She reports some feeling is present. Her visual memory has not returned.

1.54. She is quite flushed. When queried about degree of feeling she was unable to know because of the flushing and burning feeling.

2.05. Visually objects are quiet but still stand out in sharp relief. She reports that the nicotinic acid has helped her.

2.17. Slight visual changes still present. She feels no better but appears more alert.

2.23. She was momentarily uncertain whether she had had any experience. Now she reports some slight appreciation of music.

2.32. Subject complains she is cold. The visual changes are nearly gone. She was given 1 gram ascorbic acid by mouth. She thought it was more nicotinic acid but did not care.

2.52. She had lunch consisting of an egg sandwich and a cup of coffee. The egg tasted like egg only on the third mouthful.

3.04. Subject shivered and still feels cold.

3.24. As above.

3.40. The flush due to nicotinic acid is still present but she is cold. Pupils are 1/3. Her fingers are cyanosed.

4.20. Subject still is flushed and cold. She remains without any feeling, being neither depressed nor happy.

4.45. Her legs are now flushed and she is less chilly.

5.10. She is able to think more clearly and to follow conversation. Vision is normal. She appears more normal than at any time during the experience.

6.00. She ate soup and toast at a friend's home. There was no emotional reaction. At her own home she was given 400 mg. Tuinal. She noted she was not able to close her eyes.

7.00. As she was not asleep or sleepy she was given 200 mg. Tuinal. Finally after two cocktails she fell asleep while watching television at 9.30. Once during this period she felt she would never again be able to feel but this did not depress her.

Report by Subject

The following account was written six weeks after the experiment.

I took penicillamine Saturday and Sunday as ordered and with the effects as reported. When I came to the office to take LSD-25, I felt rather sick, due to the clinging odour and some nausea. I expected nothing much would happen during the experience. I was not tense, I just wanted to get the experience over with so I could be finished with the penicillamine.

I took the LSD-25 at 9.15 a.m. During the next hour I had a fleeting feeling of tingling in my hands and the typical LSD-25 feeling behind my eyes. Also there were moments when detail stood out more clearly but these were not sustained. I was terribly aware of the odour and felt nauseated. This feeling compared with the nausea I experienced over the weekend and was not like the fluttery feeling usual for me after LSD-25. Toward the end of the hour I became restless and more sickened by the horrible odour. During the second hour I began feeling quite cold and I think I remained cold until about noon. When I closed my eyes I envisioned mounds of ulcerative decaying flesh. I felt it strange that this imagery should not be repulsive to me or frighten me—I merely noted and reported it. This imagery came in waves for a short time and seemed to me to relate to the odour. Following this, I noted very slight visual changes, mainly in lighting and depth perception within the room. Music was playing and I was aware of it but not responsive to it. I remember remarking that when some Mexican music was playing I would expect to imagine fat paunchy little people but this was not the case now. It became a bit difficult for me to think clearly, but there was no overall time distortion. About one and a half hours after I took LSD-25, I began having marked visual distortions which I associated with former experiences. The striking differences were that (1) they were not preceded by the usual shimmering effect, (2) they were clear-cut distortions of pattern and depth rather than an effect superimposed on a surface, (3) the distortions did not take the form of human beings and that (4) they elicited no emotional response from me. As these changes became more marked, I became unaware of the odour and of my body. During the next hour this visual flow was very striking and fast moving. Music was played throughout and I was quite aware of it but not involved in it in any way. When I looked at the record player I was very sensitive to the sight of the record turning around and the spots of dust jumping up and down. I was asked to try to leave my body but this I could not do. I was entirely unaware of my body, I could neither feel nor imagine, so (to me) actually there was no "me"; I did not exist. During this time the experience consisted of one area where visual changes were occurring and one area where music was being played. There was no relation one to the other and I was merely an instrument noting these facts like a camera making an impression on a negative.

Shortly after noon I could make out an animal from a distortion of the drapes so I commented on this, saying I was coming out of it. Soon after this I could make out two people leading a horse and for the first time I had a fleeting surge of feeling (interest) and thought my emotions would return. I said I was definitely coming out of the experience and waited for a flood of emotions. The visual flow slowed down. I became aware of my body and aware that I was now warm. (I had wrapped myself in a blanket in a most uncomfortable position, so I now removed it and made myself comfortable.) During the next half hour the two areas became three areas—i.e. visual, sound and body—but there was no harmony between them and each existed as a separate entity. One of the visual effects that was most marked now was a distinct stroboscopic effect of movement. I had never seen it to this degree before. I commented upon it as a neutral observer would. Also there was marked after image seen peripherally.

Between 1 p.m. and 2 p.m. I became aware, once more, of the unpleasant odour but it did not overpower me as earlier. I noticed it mainly when I voided. The visual flow subsided but detail stood out very clearly still. I was given 1 gm. of nicotinic acid by mouth which I took automatically—I had protested vehemently on previous occasions when I had had LSD-25. The flush that followed was not unpleasant. In fact, I was unaware of it unless my attention was drawn to it. It lasted an unusually long time and I remember when I got ready for bed at about 6 p.m. I noted my body was still flushed. (My normal flush from nicotinic acid lasts about one hour.) During this period I knew my emotional tone had not returned. I tried to visualize the faces of my friends, as I normally can when I think of them, and have always been able to do in previous LSD-25 experiences, but was totally unable to do this.

Following this, I began to have a feeling of uncertainty as to whether or not I had been the one who had the experience. The visual changes had lessened considerably, but I was still without feeling. This did not worry me at all, I merely reported it as unusual. It became necessary for me to produce another specimen of urine for the laboratory but I was unable to do this, and this too I found strange. I was given a cup of coffee which tasted like coffee and an egg sandwich which I could identify as egg but otherwise was not tasty. I consumed this lunch automatically. I still found it hard to comprehend conversation directed toward me, but followed short orders like an automat. I began to feel chilly again and this continued until I went to sleep that night. At no time did I recognize myself as feeling tired, which is quite unusual for me following a long LSD-25 experience.

I was taken to a friend's home for supper—part of which I consumed. While there, I could correctly identify the feelings of those around me, but was not able to respond to them. I felt confused by so many people and so much activity, so I quickly gave up eating and asked to be taken home.

I was given 400 mg. Tuinal at 6 p.m. and went to bed but was unable to keep my eyes closed and go to sleep. About 7 p.m., I believe, I was given 200 mg. more of Tuinal. Until I went to sleep about 9.30 p.m. or so, I had in addition two cocktails of rum and coke. I remember expressing the idea that since I was unable to "feel" I would never be able to sleep again either. I was out of bed and walking around twice that I know of between 9.30 p.m. and 1.0 a.m.—that it, I awakened up and walked around a bit, sat in the living room and watched

T.V. for a short while. I slept soundly from 1.0 a.m. to 9.0 a.m. the next morning. At that time I walked around a bit again, then returned to bed and slept until noon.

AFTERMATH

1st Phase—Tuesday to Friday inclusive (Days 1 to 4)

Two months after the experiment the subject wrote as follows:

I call this the stage of "automatic behaviour". I came to work automatically, ate at the proper time, pin-curlled my hair in the evenings and went to bed at the appropriate time, etc. In the morning at work I would do routine things as soon as I arrived, but during the rest of the day I just sat at my desk doing nothing. If anyone gave me a simple task I could do it, but when that was finished I would resume my sitting. I was quite aware of the people around me and could identify their feelings but did not respond to these feelings. (My co-workers were either frightened, worried, or felt sorry for me. In general, they felt uncomfortable in my presence.) I had no initiative or interest in anything. I had difficulty in following conversation and realized my thinking was not normal and that my judgment was impaired. This did not worry me but being aware of it I checked and rechecked the few things I did to be sure they were correct. I could relate superficially to one person and even to two people if I could watch them closely. In order not to appear too strange to people, I used my past experiences as clues or guides to outward appropriate behaviour. If more than two people were present, this broke down. I became confused, gave up all pretence of being a social animal and retreated within myself.

In the evenings I watched TV continuously—no matter what programme was being shown. Usually I could not follow the content very well and at no time did any programme have an emotional impact on me. The only time I turned the radio on was to listen to news broadcasts and then would turn it off immediately. Some of the news items stuck with me—others did not even register. My pattern of reading was entirely changed. Usually I read two to three books (novels) a week and although I had some new ones at home I never picked them up. Instead I read the newspapers more thoroughly than I ever did before in my life. Even an out of town newspaper which I take kept me active for hours reading all the classified ads. I remember one night when I never slept at all sitting up in bed from about 2.0 to 5.0 a.m. reading the one paper.

Physically, the major thing I noticed was the progressive dryness of my mucous membranes and skin. During this period the main discomfort from this was the fact that I could not keep my "gritty" eyes closed. My lids would fall naturally about half-way down but beyond that I had to force them and they tended to fly up again. I found it quite strange to attempt to fall asleep with my eyes partly open and this may have had some effect on my sleep pattern. The other thing I noticed was that I frequently felt chilly.

Verbal communication was full of pitfalls. I never realized before that the English language is full of "loaded" words, that is, so many words have an emotional value. I was unable to use these words and as a result my conversation was very stilted and what I would call formal. I could use none of the ordinary social amenities—no please, thank you, or hello, etc. On one occasion, one of my colleagues gave me an unusual box of matches. I felt I could not keep it because he would then expect at least a thank you. I did not know what to do, when suddenly I heard myself saying: "I don't require matches. I have a lighter." When I say I heard myself, it was exactly that. I did not plan in advance what to say on these occasions and it sounded like a tape playing back my voice. I quite recognized my style of speech was strange for me and noted it as unusual but otherwise was not concerned about the situation.

During this entire period, I recognized the fact that I was devoid of feeling, my thinking was impoverished and somewhat confused, my judgment was impaired and that I had never been in this state before. I believed it had come about because I had taken this particular combination of drugs. However, I believed this to be irreversible and was not in the least concerned about it. From time to time Dr. H. would explain to me what he felt had happened and predict the course it might take. I would either agree or disagree with him, but it was as if we were discussing a patient, not myself.

The following notes were made by the observers on the days indicated.

First Day. The subject awakened at 9.30 a.m. but slept again until 1.00 p.m. She then came to work at 3.00. Her face was very pale and her pupils were pin-point (less than $1/4$). She reported that she was able to think clearly but did not know whether or not feeling was present. Slight visual changes remained. She still saw the drapery stand out very sharply in relief. She remained without feeling all day.

Second Day. Although she felt somewhat better than the previous day, little emotion was present. In the evening she said she would be sad if she could

feel but there was no real sadness in her. She consumed three cocktails at home but noted no effect and then took 100 mg. seconal at 11.30 p.m.

Third Day. She awakened at 7.18 a.m. and then slept again until 9.00 a.m. No feeling was present. She came to work but could not accomplish anything. To the senior author she appeared to be in a serious psychotic depression. However, she denied being depressed. Her reaction seemed so similar to a reserpine-induced depression that she was given 10 mg. dextedrine by mouth at 1.30 p.m. In one half hour speech was more spontaneous. At 2.08, the tension so apparent in her face began to lift. At 2.20, all her face felt normal except for a band-like area encircling her head. Her face regained some colour. At 2.30, she reported a momentary feeling of interest in life. At 5.00, she drove home in her car and at 6.00 had dinner with friends. Before dinner she took a 15 mg. dextedrine spansule. The experience during dinner was dreadful because she had no feeling and was not able to engage in conversation with other members of the dinner group. At 7.30, the inner tremor she had felt the day she had received LSD-25 returned and she was very chilly for nearly one hour. Suddenly she felt reasonably good and was able to talk more freely. However she remained cold all evening. She took 100 mg. sodium seconal at 12.00 midnight, but did not sleep. At 3.15 a.m. she took another 100 mg.; at 4.00, she developed an odd feeling which she decided one half hour later was hunger. She then ate a substantial lunch. Following this, she took a prolonged hot bath, ate some more and went to work at 9.35 a.m.

Fourth Day. She reported she had some feeling this morning, could talk fairly well and was able to relate to people more appropriately but felt very formal with them. She expressed some optimism that she might eventually be normal. The drapes had lost their tapestry-like appearance and appeared normal. She had vague momentary feelings of well-being. A laboratory test she had ordered was ruined. There was no reaction from her whereas normally she would have been very much annoyed and irritated by this.

She remained this way until noon when she drove home for lunch. She had no appetite and did not enjoy eating. The news on the radio had no meaning for her and driving back to work she could not remember what had been said. After lunch she felt she was better than yesterday because she was able to experience some tension now and then. Toward mid-afternoon she became more and more withdrawn until she reached her lowest point at 3.00. She was now very cold and was given 10 mg. dextedrine. At 5.00 p.m. she was able to talk better. There was no change the rest of the day.

2nd Phase—Saturday to Thursday (Day 5 to 10)

The subject called this phase the stage of suspended animation.

Fifth Day. Saturday morning about 11 a.m., I began to feel extremely cold. I had the thermostat set at 80°, was in bed wearing a flannelette nightgown and had a heating pad turned on high. As time went on I got colder and colder. The sun was shining brilliantly through the venetian blinds and I was lying on my side with my eyes open facing the sun (usually I lie on the other side). I don't know how long I remained there motionless, but it was at least two hours and probably closer to four hours. I believed I would die and judged myself to be about three-quarters dead at that time. I was not at all disturbed by this—merely waited for the last quarter to go. I was given medication and eventually warmed up.

She was seen on the fifth day at home. She was very cold, cyanosed and her hands were cold to touch. Her pupils were pin-point. Pulse was 60.

No feeling was present. She took 5 mg. methedrine about 3.30 p.m. and read for awhile. About 3.50 she suddenly became very warm with a prickly

sensation in her skin similar to a mild nicotinic acid flush. She became more comfortable and had a twilight sleep with hypnagogic phenomena. One half hour later she was awakened by one hand falling asleep. She still was comfortable and felt relaxed with her eyes closed until 5.00 p.m. She felt warm. Pupils were pin-point. This was the first time she had been able to keep her eyes normally closed while awake and resting. She felt she had some positive feelings. Her skin was very dry. At 6.00 p.m. she became chilly and took 10 mg. methedrine. At 6.40 she was really hot; at 7.55 her hands were wet (first perspiration all week). At 9.00 she was still warm and her hands moist. She watched television all evening but with no interest. It was something to do. The programmes were dull. She was able to follow the story, but when watching hockey could not remember which side was winning. At 11.30 p.m. there was no further change. Pupils were $1/8$. She washed her face and watered the plants. At 12.45, she took 400 mg. Tuinal and a cocktail and slept by 1.45 a.m.

Sixth Day. She slept well and awakened by 11.15 a.m. She was warm, pupils were $1/4$ to $1/3$. She felt alive and alert but now noted some trace of penicillamine odour. At 12.45 she ate a lunch of tea and toast and then noted she had less of the alive and well-being feeling. Although she was regressing she remained warm and her palms were moist. Her eyes were tired. At 1.40 p.m. she took 5 mg. methedrine. At 2.35 she was very hot and felt as if she was perspiring and itchy but there was no perspiration. The hot feeling was present momentarily. At 3.45 she was invited out for dinner but was very uncertain how she would react to people. Pulse 78. At 4.35 she noted she was getting colder and took 5 mg. methedrine. She felt weak and shaky for two hours as though this was the first day up after being confined to bed for several days. Pulse 70. At 5.15, her hands were warm but her feet were cold. She did not feel alive but felt better than yesterday. 8.30—During dinner she was able to talk fairly well at first but this became more difficult later on. About 7.15 became cold which was marked by 8.30. Her right eye ached severely. Pupils were pin point. No feeling was present. She took 10 mg. methedrine. At 9.10 she was warmer but her hands were cold. At 10.30 she was hot, her eyes were normal. Pulse was 90. 10.40—400 mg. Tuinal and slept until 4.00 a.m. She was extremely restless so took Tuinal 200 mg. and slept until 11.00.

Following this experience, during this second phase, the outstanding thing was this awful cold. When I felt myself starting to become cold, I became mobilized to do something to prevent it. This was much more important to me than the loss of feeling tone. The automatic quality of my behaviour disappeared to a large extent. I did not go to work unless I was told to. I no longer pincurled my hair. I did eat fairly appropriately, because I felt this might prevent my getting cold. My thinking was still confused and became even more concrete. My judgment was more impaired and I felt very uncertain of my ability to comprehend and remember. I made copious notes related to medication and its effects on me. I felt it necessary to have definite directions written regarding medication. I asked for guidance continually as to what I should do and when.

My mucous membranes became so dry as to cause actual physical discomfort. My nose bothered me terribly and my eyes ached. Food had no taste and at times it was difficult to force it down, my mouth was so dry. I drank large quantities of fluid.

Towards the end of this time, when I was warm I would think that perhaps I might be able to feel again sometime in the future, but when I was cold I would again think this was irreversible. However, the cold spells became more infrequent which in turn fostered the belief that I would become normal. The last day of this phase I remember remarking to someone that if I ever smiled again I felt my face would crack, it felt so set and rigid. That night my jaws started aching noticeably and this lasted all evening.

Following are some further excerpts from the subject's notes made during this phase.

Seventh Day. 3.25 p.m. Pupils 1/4 to 1/3. Have been reading articles in a magazine without interest but am able to follow it quite well. Have not experienced that very cold feeling of Saturday or the chill of last night. Pulse 80. Find it hard to compare my state to any day but Saturday. Emotion or its lack does not seem important rather the physiological condition. Saturday was the worst day because of the physical coldness with the absence of any feeling. This was like a dead feeling. I have not recognized any tension since Friday.

6.0 p.m. Ascorbic acid 1 gm. I am having a sensation which I can only call one of anticipation, as though my system was ready for an emergency. I do not know whether to take methedrine. It is practically impossible to judge after all these days, as long as my body is comfortable; when the freezing cold is present I know. I am now warm except for my feet. Surely it won't hurt if I wait until 7.0 p.m. to take methedrine.

7.0 p.m. Have had 1½ drinks of rye and feel inebriated—unusual for me except maybe my nutrition is not what it should be. Eating a hotdog. Feel neither depressed nor happy. Have not any judgment about taking methedrine so will not take any.

10.30 p.m. Confused about instructions doctor left me. Tuinal 200 mg.

11.0 p.m. My reasoning seems to be off. Last night I needed 600 mg. Tuinal so why do I think 200 mg. will do now? This is the first day which has seemed so long. It has not been boring. Will set my alarm for 8.30 a.m. and if I feel well will be at work by 10.30.

Eighth Day. 2.35 p.m. Hands cold for some time now. Not as good this afternoon. Either the room or I am getting cold.

3.20 p.m. Ten mg. methedrine.

4.0 p.m. Rushed home—very cold and stated if I do not get home now may not make it.

Ninth Day. 3.30 p.m. Propane gas people were changing tanks next door causing quite a commotion. I became quite apprehensive and although I felt sure that was what was going on, I got up and looked out. I don't think I would have done this a couple of days ago.

10.0 p.m. Feel a desire to communicate with people. Would phone R. but am afraid I wouldn't have anything to say.

The observers noted the following:

Tenth Day. 10.30 a.m. Coffee. Started to feel cold. Methedrine 10 mg. Pupils pin-point.

10.50. Two inhalations med-adrenaline (200 µg.)*.

11.00. No effect. Two more inhalations.

11.05. Faint flush on face visible. Slight feeling of warmth. Warming up.

11.14. Getting chilly again.

11.25. Chilly, shivery.

11.28. Pulse 70. Pupils pin-point.

11.30. Warming up.

11.34. Still warmer. Pulse 74. Pupils 1/4.

12.00 noon. Warm inside.

12.40 p.m. Have been sneezing and blowing my nose ever since arriving home. Have a sensation of something bothering my nostril. Can't stop sneezing long enough to make lunch.

12.50 p.m. Not sneezing now but still blowing an amazing quantity. Sensation still there but not as marked.

1.05 p.m. Eating lunch but still blowing just as if I had a very bad head cold which I haven't. Feel warm.

1.25 p.m. Still blowing and sneezing. Pupils 1/4. Pulse 76.

2.0 p.m. Starting to feel chilly. Still sneezing and blowing. Maybe a cold is starting.

2.03 p.m. Two inhalations of adrenaline. An immediate reaction, heart pounding. Pulse

78. Pupils 1/4.

2.08 p.m. Pulse 82. Still shaky but not so badly. Heart still pounding. Pupils unchanged.

2.13 p.m. Pulse 80. Body feels warm but hands are cold.

2.15 p.m. No more sneezing although blowing nose occasionally. Chest feels a bit tight.

2.25 p.m. Pulse 80.

2.50 p.m. Blowing nose almost continually. Feel warm. Pupils 1/4.

3.0 p.m. Real warm but not perspiring. Pupils 1/4. Ten mg. methedrine (as ordered).

4.30 p.m. Pulse 76. Warm. Have not blown my nose for ten minutes. Longest period of time.

6.0 p.m. Sneezing again and more nasal discharge. Ten mg. methedrine. My eyes have been bothering me as though I were stuffed up with a cold for some time now.

6.30 p.m. Pupils 1/6. Really believe I have a cold. Sneezing, coughing and blowing.

If this was a cold, I would be perspiring but am not. Jaws are aching.

* Medihaler—Riker.

11.30 p.m. Not sleepy. No perspiration. Quite warm at times. Still considerable discharge but very watery especially when I bend my head. Eyes feel heavy and sinuses below are aching dully. A strange thing is that my nose runs and I am unaware of it until I feel it on skin near my lip. Everything about this business is strange. Think I have some feeling and am certainly not depressed.

3rd Phase—Following Three Weeks (Days 11–35)

The subject described this period of time as follows:

I call this the stage of "recovery". Friday morning when I awakened I felt alive and alert. At work, this feeling of well-being became stronger and my emotions seemed to awaken. By noon time I was talking easily with people, joking and laughing. I felt quite happy that I could feel again. During the next several days I felt completely exhausted. The slightest exertion caused an increase in pulse rate, shortness of breath and tightness of chest, feeling of weakness and shakiness. There was no perspiration accompanying this. My eyes and mucous membranes were still dry. This continued for the next 3–4 days then the muscles of my neck and shoulders ached for a few days.

I began to read novels again with interest and also to enjoy TV and music.

During the next week, at times I felt chilly, but usually within an hour I warmed up without medication. When I felt cold my pupils were small but when warm, they dilated to about 1/3. Toward the end of the week, these episodes were less frequent.

My mood was good throughout but I did experience annoyance appropriately. I felt I could not yet empathize normally, but could at least do lip service. I did not experience any other emotion, nor did I worry when this was indicated.

I slept well and felt alert during the daytime. My appetite did not return but as my salivary glands started to function normally once more I had less difficulty in eating.

The second week of this phase found my mucous membranes all right except for my eyes. Outside in the cold there was some slight watering, but other than that they were very dry and ached easily. I gradually resumed my normal interests, showed initiative again and my thinking cleared up totally.

Further excerpts from the daily notes are given.

Eleventh day. 12.0 noon. Returned from work and have made my lunch. Felt increasingly good this a.m. Could relate quite well with people. Talked with G. for about five minutes and joked and laughed with him. I felt almost hot when talking with G. and my palms were wet. Nose running again—no discharge while I was out in the cold.

1.30 p.m. Feel chilly, not real cold. Methedrine 10 mg.

1.40 p.m. Pulse 80.

2.10 p.m. Still chilly.

2.40 p.m. Still chilly. Pupils 1/4. Much less nasal discharge—when I'm cold it lessens and vice versa. Pulse 72.

3.55 p.m. Warmed up immediately after last note and slept until 5 minutes ago. Am comfortable now. Pupils 1/6.

5.30 p.m. Cleaned up and ready to go to H. for dinner. Talked with R. and L. on the phone quite easily. Pupils 1/3. Warm.

6.30 p.m. At H. After about 20 minutes felt chilly. Methedrine 10 mg. Talked easily, laughed and joked. About 7.20 p.m. felt very warm. As time went on felt some strain at carrying on conversation. Didn't have an appetite but ate a good dinner. Felt coolish off and on and quite tired by the time I left about 8.30 p.m. Mood good.

9.0 p.m. Warm and happy.

Twelfth Day (24 January, 1959). 12.45 a.m. I think I'm trying to fight off sleep so I can enjoy this renewed sensation of living. Have been quite warm all evening since I came home. Very little nasal discharge. Skin still very dry. Have rubbed buckets of lotion into it in the last few days. What a wonderful sensation it is to feel again! I've been overwhelmed by my emotions all evening. My question is now—can I feel sorrow? Maybe I'll find out at the play tomorrow night.

1.30 a.m. Have been reading Shaw's letters. Not very interesting. Did this to prevent thinking and feeling my emotions. Am very tired but not sleepy; however, I shall turn out the light now and try to sleep.

4.25 a.m. Light sleep until 4 a.m. when I wakened with the extreme restlessness I had once before. Tossing all over bed. This time I was very hot and heart pounding. Got up now and took Seconal 100 mg. and a glass of milk. Pupils pin point.

5.0 a.m. Turned off light and went to sleep shortly after.

1.40 p.m. Have been working on a business letter and find this quite a stress. I feel cold and my chest feels tight. Pupils are 1/3. Pulse 70. Methedrine 10 mg. and lunch and a break from the letter.

2.05 p.m. Starting to warm up now. Pulse 80.

5.30 p.m. Have been all afternoon writing the one letter. Remained warm—no difficulty in thinking. Affect appropriate. Very little nasal discharge, instead, mucous membranes very dry again.

6.05 p.m. Methedrine 10 mg. Starting to feel chilly. Were I not going out tonight I would try to wait it out (delay taking the methedrine) but at the moment I don't feel up to watching a play. Pupils 1/6. Pulse 68. I feel all used up emotionally after writing the letter, as well as very tired.

6.40 p.m. No change noted as yet. Have been reading the paper but have not absorbed what I read—not like before when I couldn't comprehend and had to keep going back over it—as though I have not the energy really to read and understand. Do I feel a bit low? Perhaps—to me it is being very tired, but that might be a camouflage. Pupils 1/6–1/4, pulse 76. My nose is bothering me terribly—it is so dry. One extreme to the other.

6.50 p.m. Suddenly I'm warm again.

7.15 p.m. Still I feel absolutely beat. Phoned R. to cancel tonight's arrangements. Haven't the energy to get dressed, let alone watch a highly emotional play. Eating supper was a terrific chore—I had to stuff down each mouthful of the meat pie.

8.20 p.m. Still exhausted. Feel as though there is pressure in left epigastric area that causes me to force my breathing. Pupils 1/4. Pulse 80. Nose still bothering me—extremely dry.

9.20 p.m. Breathing less of an effort now. Don't feel quite so tired. I really can't see any depressive feelings—just used up too much adrenaline writing letter, I guess.

10.0 p.m. Am rather passively enjoying the Perry Como show—first enjoyment I have received from TV during this siege. I note any physical exertion, even walking to and from the kitchen causes a sudden surge of heat in my body and a feeling of weakness.

1.40 a.m. Tuinal 200 mg. Feel badly about being such a chicken to take the Tuinal but don't look forward to such a night as last night. Feel I can't cope with this sudden surge of emotions adequately. Guess I'm afraid I may become terribly depressed and may do something impulsively. Am now in bed and will try to read.

Thirteenth Day. Just remembered I had a very beautiful dream last night—in colour—the colour did not make it beautiful, it was the emotional content.

2.55 p.m. What a difference watching the golf today on TV and last Sunday. I sure had no trouble following it, knowing the number of strokes, etc. I became highly involved (rather resented having to make notes through it) so much so that when T. missed the tying putt at the end I jumped right up on the chesterfield involuntarily.

4.0 p.m. Have washed my hair and had a bath. Great exertion. Feeling of tightness across diaphragm. Shaky. Breathing heavily. General feeling of weakness. Pupils 1/3. Pulse 106 after resting for 5 minutes.

4.05 p.m. Pulse 102. Tightness still present. Not as shaky now.

4.15 p.m. Feeling better now. The main thing differentiating this from an ordinary extreme weakness is the lack of perspiration. Pulse 102.

5.15 p.m. Tightness gone. Pulse 82. Have just been resting the past hour and feel quite O.K. now. Pupils 1/4.

6.0 p.m. Least bit of exertion causes a feeling of weakness. Am washing out some lingerie and I have to keep resting while I soak it. Nose very dry now and causing some discomfort.

Fourteenth Day. Turned out light at 12.40 a.m. Had a rotten night's sleep. Seems to me it was hours before I began dozing. Thought of taking seconal but was quite content to lie there even if I didn't sleep at all. When I did sleep it seemed like just dozing to me.

7.45 a.m. At the moment, I do not feel at all rested and it has taken me half an hour to even get started. Feel quite warm. Had several unspectacular dreams.

9.10 a.m. At work. Feel weak. Out of puff and very warm from exertion of coming to work.

9.45 a.m. Feeling of weakness has passed away now. Am doing my regular work with interest. No difficulty in thinking.

10.0 a.m. Starting to feel chilly. Notice now I am first aware of this feeling in the lower parts of my body, rather than hands and arms first, as previously noted.

11.40 a.m. Noticed while walking down corridor a peculiar sensation about my eyes—feel my pupils should be widely dilated—sort of a film before my eyes—pupils are between 1/4–1/6.

12.25 p.m. At home, eyes O.K. now but they feel tired. Muscles across shoulders are aching badly. Mucous membranes of nose dryer than at any other time today.

Fifteenth Day. 7.30 a.m. Up—still sleepy and groggy.

8.15 a.m. Having breakfast now. More alert. Nicely warm. Pupils pin point. Mood seems to be good. Yawning a lot (normal for me in a.m.) which I don't remember doing during these past two weeks. I find real pleasure in yawning and stretching now. It is amazing what simple things give pleasure after such an experience.

8.30 p.m. Pupils 1/4.

1.30 p.m. Back to work after lunch. I have always been sensitive to brilliant sunshine but today the sun at noon caused actual pain in my eyes—they did not water at all—even the sun hitting my peripheral vision caused pain. Wore sun glasses back to work with considerable relief. Did some chores at noon without exhaustion.

2.0 p.m. I read about six pages of handwriting on a chart and my eyes feel very strained—almost to the point of causing vague dizziness—a pulling sensation. Mucous membrane of nose causing little or no discomfort today. Thinking and activity normal tempo.

Sixteenth Day. 7.30 a.m. Had difficulty getting to sleep—eyes so dry I couldn't keep them closed, more comfortable slightly open. Thought I had extreme restlessness with some panic about 5.15 a.m. but this may have been a nightmare—I'm no longer sure. Feel tired and sleepy this a.m.—hard to waken and get going. Quite warm. Nose a bit stuffed up. Pupils 1/6–1/4.

9.40 a.m. Have been at work since 9.0 a.m. No fatigue. Warm. Spirits good. Alert and interested. Pupils 1/6. Forgot to note last night my sense of smell was hyperacute. Lying in bed, trying to sleep, was very sensitive to the smell of my table lighter beside the bed. This has occurred once or twice before in the last week as well.

As of yesterday the outside temperature was -35° F. and my eyes still did not water, nose very slightly runny outside. When I returned from lunch today -31° F. with bright sunlight a tear formed and fell from right eye. Left eye remained dry.

Twenty-First Day. 9.30 a.m. At work—mood good, no sedative hangover. Realize today my emotional tone is still not normal for me. Have felt happy and even irritable (appropriately) but never sad nor anxious even though warranted. My feeling of empathy is still practically totally lacking. I can identify feelings around me but cannot experience these feelings in the situation. Right eye has slight bit of moisture but left eye has none.

Evening—eyes unchanged. Remembered that during the week-end I still did not have my normal response to the music which I usually like. Found myself reading instead of listening to a band I like on T.V. Even when a bongo drummer came on I neither watched nor listened. I was aware of it, but no response. Still have no appetite—eat mechanically at meal time.

Twenty-third Day. Not sad nor anxious—unable to worry. Can use the terms to express these other emotions, e.g. I'm sorry—but this is really lip service. Nose has been quite normal for past three days since Monday a.m.

Twenty-ninth Day. My eyes ached very badly all evening, interfered with reading and to a lesser degree watching TV. When I went to bed again, as some time ago, I couldn't close my eyes properly to sleep—as well there was a dull ache in area of antrums above eyes. At 12.30 a.m. decided if I weren't asleep by 1.0 a.m. would take sedation. At 1.0 a.m. decided to wait until 1.30 a.m.—during this time fell asleep as far as I know with eyes slightly open. A.m.—to work—feel refreshed. Mood good. Eyes dry.

Thirty-first Day. Amount of moisture in eyes still not normal. Occasionally when smoke gets in them or I laugh excessively I can feel moisture—otherwise no. Eyes still tired in evenings. Mood has remained on the whole, very good. Yesterday I worked hard all afternoon and evening cleaning house, polishing, doing a washing and all the dishes. Was not tired at all and interest remained high throughout. This is a first since January 10th!

Fourth Phase—Residual Effects Two Months Later

At this time I still have not experienced any feeling of sadness, anxiety or worry. Events have occurred during this period which normally would have resulted in one of these feelings. My ability to empathize has improved but is not present to the same degree as previously.

I sleep well and eat adequately although only rarely have I felt hungry. I seldom feel tired and have my normal energy. My interest is high in my work and at home.

My eyes still bother me and remain very dry except in a cold wind. They ache quite frequently and I find I am unable to read as much as I could before.

I find I feel chilly in the evenings, and keep the thermostat set higher in my house than I ever did before. In the daytime I'm usually quite warm.

The after-effects of this experience compared with my two former experiences with LSD-25 were quite striking. The first time I took LSD-25 was in 1954 and I remember it very vividly. It was largely a perceptual experience and I reacted strongly to all stimuli. The second time I took LSD-25 was one year ago. This time it resembled a transcendental experience and again remains very vivid in my memory. The visual distortions were of a minor nature, but the emotional charge was great. This last time the whole experience seems as though it had happened to someone else. When I concentrate on it I can recall the striking imagery but it has no impact on me even yet. It is easier to recall the total lack of emotion, but again this is still unreal to me. I can distinctly recall the Saturday morning when I felt I was almost dead, but this seems to have been someone else lying in bed dying—not me. It is very hard for me to realize that those two or three weeks happened in my life and as time goes on it is developing a dream-like quality. On the other hand, it is still very real to my close friends, who tried to relate to me in this strange state.*

* The subject was seen on several occasions by a couple who had known her for ten years (Dr. D. G. McKerracher, Professor of Psychiatry, University of Saskatchewan, and Mrs. McKerracher, a former Psychiatric Nurse). They report as follows:

"On the first night her telephone conversation appeared unaccustomedly formal and stilted.

"On the third night at supper with our family, she was ill at ease, uncomfortable and quite uncommunicative. Later she complained of being chilly, although the room was quite warm. She discussed her experience impersonally and without emotion. She spoke of her lack of feeling and inability to relate to people as if discussing the condition of someone else. She was so detached that we questioned her ability to drive home alone.

"On the sixth day she again visited us. There had been no change from her stilted, formal, rigid manner of three days before. Her conduct now seemed more noticeable, more bizarre, possibly because more people were present. All were amazed and disturbed at her behaviour. When informed that a member of our family had been injured, she showed no evidence of concern.

"During the next week, contacts were by phone. There was no evidence of change; she continued to complain of coldness and dryness of the eyes. She expressed no anxiety about her symptoms, these being described as if they were those of another.

"On the eleventh day, she was next seen. At that time her manner was quite different—she was moderately spontaneous, friendly and accessible."

Five Months Later

My spirits have remained quite high. I can feel happiness and anger appropriately. On the other hand, I have not yet experienced sadness, nor have I worried when the situation warranted concern. I seem to have an abundant amount of energy. I am always more energetic in the spring than at any other time of the year, but this year it seems different. I have worked in the garden until my muscles ached but still enjoyed the work and have not felt fatigued at the end of the day. Perhaps this accounts in part for my greater interest in recreational activities this year as compared with the last few years.

My ability to empathize emotionally has not been normal since the experience. It depends upon the situation. I am able to empathize to some degree with someone who is happy although the experience is for me qualitatively different and is more superficial. However, I can only be aware intellectually of others' sadness or depression. There is no equivalent feeling in myself for the other person.

My eyes are normally moist but still tire fairly easily. In the evenings I find I have to hold books, etc., farther from me to read with ease. It is practically impossible for me to thread a needle at night, whereas I used to be able to do this quite easily.

Rarely have I felt hungry. I usually consume an adequate diet but without any real enjoyment. I have lost seven pounds of excess weight. I sleep well.

I can recall the entire period but it still seems as though it happened to someone else and that I was merely an observer.

SEQUENCE OF RECOVERY

The subject did not recover uniformly in all areas of thought, mood, activity and automatic reactivity. Thinking was not normal by the second day and power to concentrate was defective at day four. The subject remained indecisive about two weeks nor did she trust her memory. Medical instructions about taking methedrine and sleeping sedatives were all written on paper for her. She kept careful notes with times because she was instructed to do so. Visual perception became normal by day four. At this time drapes lost their three-dimensional quality and looked like drapery rather than tapestry. Emotion began to return on day eleven. During this interval, there were periods of feeling only after taking methedrine. The autonomic nervous system was not normal by day fourteen.

DISCUSSION OF BIOCHEMICAL FACTORS

1. Response to Sympathomimetic Amines

Dexedrine given three times did not alleviate the cold feeling although it did make it easier to talk and decreased the discomfort slightly. Methedrine given alone fifteen times in every case but one caused a feeling of warmth which ranged from mild to very hot. Her pupils opened to one-third or better, colour came back to her face and she was able to feel some stirring of emotion. Toward the end of the two week period less methedrine was required to maintain comfort. Thus day eleven required 30 mg./day, twelve 20 mg. and day thirteen and fourteen 10 mg. each.

Methedrine which resembles adrenaline slightly more than does dexedrine was much more effective in alleviating the cold feeling.

The ascorbic acid prevented methedrine from producing its usual autonomic reaction. Beyer (3) showed that ascorbic acid destroys amphetamine *in vitro*. This may account for the lack of response to the methedrine in the presence of ascorbic acid.

There was little or no response to the inhaled adrenaline on the morning of the tenth day. But later the same day an identical dose produced a typical increase in pulse rate, etc. The second inhalation in the morning initiated a copious secretion of mucous fluids which started one hour after and lasted about thirty-six hours. Before and following there was practically no secretion.

Adrenaline and other sympathomimetic amines tend to decrease nasal secretions. The reaction reported here is thus paradoxical. However, adrenaline is the neurohormone transmitter for sweat and perhaps other glands. Therefore they may have ceased to function due to an absence of adequate quantities of adrenaline which was restored momentarily by the inhaled medication.

TABLE I
Reaction to Sympathomimetic Amines

Day	Time	Total Amine (mg.)	Medication	Response
3	1.30 p.m.	25	1. Dexedrine, 10 mg.	Decreased tension, speech easier, some vasodilatation.
	6.00		2. Dexedrine, 15 mg.	No warmth but felt good, speech easier.
4	3.00 p.m.	10	1. Dexedrine, 10 mg.	Not warm, speech easier.
5	9.00 a.m.	15	1. Ascorbic acid, 1 gram	Very warm, comfortable flush.
	2.30 p.m.		2. Methedrine, 5 mg.	
			3. Ascorbic acid, 1 gram	Very hot, perspiration, flush.
	6.00		4. Methedrine, 10 mg.	
6	1.40 p.m.	20	1. Methedrine, 5 mg.	Warm and flushed after each medication.
	4.35		2. Methedrine, 5 mg.	
	8.30		3. Methedrine, 10 mg.	
7	11.00 a.m.	20	1. Methedrine, 10 mg. and ascorbic acid, 1 gram	Sluggish reaction, no flush.
	2.35 p.m.		2. Methedrine, 10 mg.	No reaction.
	6.00		3. Ascorbic acid, 1 gram	
8	10.30 a.m.	25	1. Ascorbic acid, 1 gram	No response.
	1.55 p.m.		2. Methedrine, 5 mg. and ascorbic acid, 1 gram	
	3.20		3. Methedrine, 10 mg.	No response.
	5.45		4. Methedrine, 10 mg.	No response.
9	10.45 a.m.	30	1. Methedrine, 10 mg. and ascorbic acid, 1 gram	No response.
	1.00 p.m.		2. Methedrine, 10 mg.	Very warm.
	6.00		3. Methedrine, 10 mg.	Warm.
10	8.15 a.m.	40	1. Methedrine, 10 mg.	Warm.
	10.35		2. Methedrine, 10 mg.	No response.
			Adrenaline, 400 μ g.	
	11.00		3. 200 μ g. adrenaline	Faint flush momentarily.
	2.00 p.m.		4. 200 μ g. adrenaline	Immediate reaction and warm.
	3.00		5. Methedrine, 10 mg.	Warm.
	6.00		6. Methedrine, 10 mg.	Warm.

11	8.00 a.m.	30	1. Methedrine, 10 mg.	} Warmed up after each medication.
	1.30 p.m.		2. Methedrine, 10 mg.	
	6.30		3. Methedrine, 10 mg.	
12	1.40 p.m.	20	1. Methedrine, 10 mg.	} Warm after each medication.
	6.05		2. Methedrine, 10 mg.	
13	1.15 p.m.	10	1. Methedrine, 10 mg.	Warm most of day.
14	10.10 a.m.	10	1. Methedrine, 10 mg.	Warm, flush.

TABLE II

Response to Sympathomimetic Amines

Sympathomimetic Amine	N	Response
Dexedrine	3	In each case speech easier but did not warm up.
Methedrine	15	In each case but one warmed up, flushed, pupils became dilated and became aware of some tingling of emotion.
Methedrine and ascorbic acid together	3	One reaction was sluggish and twice did not react.
Methedrine given within five hours after ascorbic acid ..	6	There was no reaction three times.
Adrenaline (200 μ g.)	1	No response.
	1	No response.
	1	Marked secretion of serous material.

A summary is given from the observer's report of day ten when she was given adrenaline. At 8.15 a.m. 10 mg. methedrine. Pupils pin-point. Warm. Took 10 mg. methedrine at 10.35. Thinking is fair. At 10.50 inhaled 200 μ g. adrenaline. At 11.00 inhaled 200 μ g. adrenaline. Nothing noted on inhalation. At 11.05 slightly warm for about ten minutes. Cold at 11.25. At 12.30 p.m. marked nasal mucous serous discharge occurred. Subject had felt fairly well except for dry tissues and chilly feeling. She compared this serous discharge with a heavy cold. At 2.03 given 200 μ g. adrenaline. In contrast to this morning there was an immediate reaction of pounding heart. Was warm by 2.13 and very warm by 3.00 but without any perspiration. At 3.00 took 10 mg. methedrine. At 6.00 10 mg. methedrine and remained warm. 8.00 felt miserable and sick but not depressed. Became convinced the copious nasal discharge was due to a cold. 11.35, 200 mg. Tuinal.

2. *Paradoxical Reaction to Sedatives*

The day of the experiment no sleep followed 400 mg. of Tuinal and four ounces of rum (60 proof), even though the subject was tired, quiet and apathetic. A further 200 mg. produced sleep only after two and one half hours.

3. *Unusual Reaction to Nicotinic Acid*

This subject has on frequent occasions experimentally taken 1 gram nicotinic acid and has a predictable vasodilator response. The flush occurs within 20 to 30 minutes and lasts up to one hour. LSD-25 alone does not alter the sequence of reaction, Hoffer (12). This time the nicotinic acid was taken at 1.27 p.m. and the subject was still flushed at 6.00 or four and one half hours later. In spite of the flush when subjects always feel very hot, this subject felt cold.

4. Secretion of Urine

LSD-25 is anti-diuretic for the first part of any experience (17). This is then followed by a period of increased diuresis during the latter half of the experience. In this instance the urinary output was markedly decreased throughout the entire first day.

5. Hypothesis

The unusual reactions may be accounted for on the assumption that the combination of penicillamine and LSD-25 produced a central and peripheral depletion of sympathomimetic amines. Penicillamine *in vitro* quickly alters adrenochrome to leuco-adrenochrome and possibly prevents an increase of adrenochrome in plasma. LSD-25 increases the secretion of adrenaline (20). Thus the combined effect of increased secretion and rapid consumption of adrenochrome could rapidly deplete the central stores of adrenaline and noradrenaline. If adrenochrome increased in the plasma, it could by a mass action effect slow the secretion of adrenaline.

Reserpine lowers amine concentration in the hypothalamus, in the adrenal gland, Holzbauer and Vogt (15) and in the fibres and ganglia of adrenergic neurones, Muscholl and Vogt (21). When the loss of noradrenaline is severe, there is no response to stimulation. There is also a decrease in arterial walls, Burn and Rand (5). Serotonin is also lowered, Pletscher, Shore and Brodie (25), but the specific effect of inactivating is more likely due to depletion of the amines. Thus only noradrenaline and adrenaline or its precursors as well as amine oxidase inhibitors reverse the reserpine effect, Carlsson, Lindquist, Magnussen and Waldeck (6), Olds and Olds (22). Everett and Toman (8) concluded depletion of serotonin does not play an important role in the behavioural deficit resulting from the active Rauwolfia compounds. John, Wenzel and Tschirgi (16) tested the ability of serotonin, mianserin, adrenaline and noradrenaline to attenuate the effects of reserpine on conditioned behaviour. Of these only adrenaline was active. Methedrine completely reversed the effect of reserpine peripherally.

Thus, it is likely the unusual autonomic response of this subject was due to a depletion of amines both peripherally and centrally. The peripheral lack of amine would account for the vasoconstriction and lack of secretion. Central depletion might account for the internal coldness, pin-point pupils and lack of emotion.

Evidence which favours this suggestion is:

- (a) Paradoxical autonomic reactions.
- (b) Remarkable response to adrenaline.
- (c) Reversal of autonomic reactions by methedrine which was more effective than by dexedrine. This resembles the reversal of the reserpine effect in animals by methedrine and of reserpine induced depressions in humans, Ayd (1).
- (d) Required two weeks to become reasonably normal. This is the time required in animals to regain normal amine levels in the brain.
- (e) Ascorbic acid which *in vitro* destroys methedrine prevented it from acting.
- (f) Sedatives are potentiated by adrenaline. Lack of adrenaline would account for the need for a large quantity of Tuinal the first day and nightly sedation for two weeks (200 to 600 mg. each night).

No one doubts the relationship of adrenaline to anxiety. Usually it is believed too much adrenaline relates to too much anxiety. If true, it is theoretically possible to have too little adrenaline and this could be associated to too little anxiety, i.e. to disinterest, apathy, and, as we have suggested here, to loss of affect.

DISCUSSION OF PSYCHOLOGICAL RESPONSE

The most striking feature of the experience was the absence of feeling which followed the LSD-25 experience. As a result the subject found herself (1) unable to relate adequately to others, (2) unable to use affect-laden words, (3) unable to respond to the emotional tempo of a group situation, (4) completely without drive.

Inability to Relate to Others

The inability of schizophrenic patients to relate to others has been described for many years. Various explanations have been offered for this depending upon the orientation of the author. The inadequacy of the subject's reaction is remarkably like the double-bind situation described by Bateson, Jackson, Haley and Weakland (2). In the double bind the schizophrenic patient has been the victim of conflicting demands upon him, one direct and the other abstract. Not knowing to which signal he may respond he becomes ill. These authors suggest that the schizophrenic patient's illness results from such a situation. The schizophrenic exhibits weakness in assigning the correct communication code to stimuli and messages. However, Bateson *et al.* do not consider the possibility that this basic fault may be within the illness and not be a result of faulty transmission. The error may be a faulty receiver. It is difficult to understand why a schizophrenic person should be so perceptive of mother's faulty signals and be so unaware of his own.

However in this subject there has never been any question of schizophrenia so that the basic difficulty in receiving and acting upon stimuli was normal until the experiment. For the next week at least the subject was unable to relate to other people in a normal way. The reason did not lie with the other people. The subject was without affect and simply could not react appropriately to the mood of the other person. Since no emotional participation was possible, there was no way of interacting except by intellectualizing. Conversation is a two-directional process where emotional cues provide the markers; when these are gone, there can be no interaction, merely a series of two-way statements.

The subject reported "one of my colleagues was returning to work for the first time after being awarded his Ph.D. I knew plans were afoot for a royal reception and that there would be a lot of horse-play. I felt doubtful of my capacity to put on an act which would remotely resemble my normal response to such a situation. I knew I could not in any sense be a part of the group, and that I would be overwhelmed and become very confused, so I did not go to work at all that morning. In the afternoon when I met him at work I said something to the effect that I would not congratulate him until I had some feeling."

A large group of words which have emotional meaning such as "thank you", etc. were no longer used by her since they had no meaning. On one occasion, the subject was offered a special box of matches. She realized that to accept she would be expected to thank the giver and found herself unable to do this. Instead she stated "I have a lighter". It is difficult to conceive of the

importance of affect in the use of words. But this experience was a striking demonstration that without emotion many words lose all value.

It was especially difficult to relate to groups. Several days after the experiment, it was possible for her to get along with one person, especially after taking methedrine. However, at this time group interaction was impossible and also dreaded. Coffee breaks are usually group sessions. The subject found these especially difficult. She could remember how she had reacted to similar situations and could sense the mood of the group as a whole. However, she felt it necessary to assess deliberately the mood of each group member in order to relate, so that groups larger than two confused her.

It is not difficult to understand how a loss or distortion of affect can produce a double-bind situation because the affective cues will be missed, distorted or not reacted to. If the ability to have emotion slips away gradually as the disease schizophrenia comes on, the patient loses all reference to an earlier period when reaction to emotion was normal. If the disease comes early in life, no such stable base has existed. Thus, loss of affect in itself can account for many manifestations of schizophrenia. Of course, schizophrenic patients do sometimes have schizophrenic mothers who might experience similar affective difficulties. The double-blind phenomena is according to our point of view a description of a situation which may be caused by a defect in the experiencing of affect.

A COMPARISON OF THE EXPERIENCE AND SCHIZOPHRENIA

Since Bleuler arbitrarily divided schizophrenic symptoms into two classes, changes in thought and affect have been considered primary and changes in gross perception, i.e. hallucinations, secondary. We do not agree that perceptual changes are secondary. There are no studies which prove which symptoms are primary in terms of onset, of importance for diagnosis or for treatment. It may be that distortion of perception destroys the usefulness of environmental cues and so destroys affect. Nevertheless, those who deny the utility of model psychosis experiments do so on these grounds. The experience described here was marked chiefly by a disorder of affect and to a lesser degree of thought.

Plant hallucinogens given alone do not deprive volunteers of affect although it is altered. This experience is the first one we know where LSD-25 so weakened affect that the subject denied its presence for nearly two weeks. However, we have seen somewhat similar reductions of affect in experiments with adrenolutin. In at least six experiments the adrenolutin produced an alteration in affect for up to two weeks duration. One of the first occurred in Dr. H. Osmond. At that time this experience appeared to be a depression. Now in reading the account (nearly five years later), it seems likely affect was lacking rather than being depressed.

The following notes are taken from Dr. Osmond's personal records at the time of the experiment.

On 2 November, 1954, H.O. was given 5 mg. adrenolutin by mouth at 6.20 p.m.

8.10 p.m. An inclination to sink quietly into myself and do just nothing, not even write, but once I start something I can keep going. It is very difficult to speak spontaneously, much easier just to sit. In spite of this I ate a good meal and took part in the conversation but it required some effort.

8.30 p.m. A flatness and great reluctance to do anything, even to think. I feel very remote. I do not have any spontaneity.

8.45 p.m. Very difficult to talk and not very easy to write.

9.0 p.m. It is so hard to realize that this is an important experiment and that a few hours ago I was keenly interested to know the results. Now I know, but it doesn't feel like knowing.

It is intellectually interesting but almost nothing else. No pleasure. No delight as there was this morning. Cut off in some curious way very hard to say.

9.10 p.m. Would like to say how interesting this is, but can muster so little interest inside me that it seems almost hypocritical to say so.

9.40 p.m. Feel a bit livelier, hardly very congenial but alert to carry on a conversation but if I talk I have no inclination to write and vice versa. Tired without being sleepy.

10.25 p.m. Feel very different now, quite alert to take part in conversation and am really thawing out and beginning to take some interest in what has happened. Taking a lively interest in the U.S. election results. It is good to be this way again.

The next day after having slept well, he wrote:

9.15 a.m. Feel flat still but cheered. Inclined to think some residue of this stuff's effect remains but would be hard to lay my finger on it.

3.30 p.m. Don't feel completely myself yet but don't know how to describe this accurately.

7.30 p.m. Have come to the conclusion that this stuff still works. This afternoon I completely forgot the hospital bazaar and was not aware that it was going on. I have never forgotten one before. I was detached from things. Tonight I feel slack and tired.

On 16 December, 1954, Dr. Osmond was given 16 mg. of adrenolutin by mouth. He reported the usual subtle changes in perception, corridors seemed extraordinarily long, voices were remote. In two hours he was peculiarly different. He was remarkably disinterested in matters that would normally have excited him. He appeared to have lost his emotional ability and seemed to be working on a flat, monotonous level. He was very quiet and preoccupied. In four hours he reported he was feeling a great deal livelier and more interested.

For the next two weeks he felt markedly different but did not report this to the senior author. Meanwhile A.H. had taken 16 mg. of adrenolutin by mouth. He continued to react and on the third day became aware of severe depression which lasted throughout the fourth day. He informed H.O. of this experience on 29 December, 1954 when he recovered. H.O. was then reasonably well but began to feel much better because these two independent and unexpected events tended to corroborate each other. It seemed likely his own prolonged reaction was due to the adrenolutin. On 26 December, 1954 he recorded in his notes:

In church I was aware of what seemed like transient fluctuations in the lighting and have noticed this last week a slight frontal headache, lethargy, some thirst with a dry mouth, a sense of detachment without it being quite unreality. I keep wondering whether this has any relationship with adrenolutin or whether it is just fed-upness with Weyburn, the hospital and the prairies where we have now been for several Christmases. Or is it just suggestion? I have always been inclined to putting things by but feel that I have done this more for the past ten days . . . I don't think I would care to be as I have been very long. It is a bloodless sort of existence.

On 28 December, he wrote:

This lethargy is foul. It hangs over one like a smoke cloud. You can't put a finger on it. It means that what one can usually do without effort now requires effort. The pleasantest thing is to let things slide. Let anything slide. Now this could simply mean that I am detaching myself from Weyburn.

On 29 December, 1954, H.O. wrote to A.H.:

And now my old zest and pleasure in life is back. Something that one never misses till it is gone. Yet how hard to be deprived of it. How abysmal to remind oneself that this or that is important because you don't *feel* that it is important but only know it intellectually. Lord Balfour's "nothing matters much and very little matters at all" may be true but it means a zestless life. Monochromatic. It will be interesting to see whether adrenolutin has had anything to do with this or whether it has just been a coincidence that I took some virus infection which began to show itself shortly after the adrenolutin. We must see.

The consequences of a very slowly excreted hallucinogen which could remain circulating and effective in a minor way would fit in well with the known facts of the insidious onset of schizophrenia. For weeks on end you could never quite put your finger on it. Was that vaguely

unpleasant feeling in the head really a headache or "just imagination" or an incipient cerebral tumour . . . In this hypochondriacal state one finds some comfort in making one's diffuse and intangible discomforts concrete. Yet can this stuff possibly have acted for fourteen days. It seems improbable but is not completely impossible. Though I would suspect that it is a cold or something that has complicated things . . . As we talked (to A.H. by long distance telephone) I felt my *joie de vivre* returning. Something that had not been possible except for fleeting intervals for fourteen days is now back and yet though it makes a vast difference to life I would be hard put to say what had happened. So there you are. I didn't tell you because I was a trifle ashamed when it was past and did not want to suggest anything to you.

Dr. Osmond's prolonged experience in many ways resembled the one which followed penicillamine and LSD-25. We believe this affectless state produced in this subject by penicillamine and LSD-25 and in H.O. by adrenolutin are useful models of natural schizophrenia. If true then it becomes obvious how important is the restoration of affect in the treatment of schizophrenia. Much more attention must be given to the role of affect and to its influence upon thought and thus on behaviour.

SUMMARY

A subject given LSD-25 after two days' treatment with penicillamine developed a psychosis characterized primarily by loss of affect for two weeks. Her two previous reactions to LSD-25 were similar to those described in the literature. We postulate that this combination of chemicals depletes the sympathomimetic amine content of the peripheral and central stores thus producing the disorder of affect as well as of autonomic reversal.

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A COMPARATIVE CONTROLLED TRIAL OF METHOTRIMEPRAZINE ("VERACTIL") IN CHRONIC SCHIZOPHRENIA

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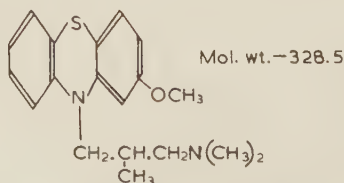
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INTRODUCTION

DESPITE the good results reported in recent years in many cases of chronic schizophrenia following the use of tranquillizing drugs, there remains in mental hospitals a group of chronic and often deteriorated patients who have shown a strong resistance to all forms of treatment. In many such cases disturbances of behaviour are modified and sometimes controlled by such drugs as chlorpromazine and reserpine. Nevertheless, the overall situation is far from satisfactory and the search for more effective drugs continues.

Methotrimeprazine has the characteristic central action of chlorpromazine, some anti-adrenaline activity and anti-histaminic properties comparable to those of promethazine.



It is prepared for clinical use by May & Baker Ltd. under the name "Veractil" in the form of its acid maleate which contains 73 per cent. of the active base.

PREVIOUS CLINICAL STUDIES

Deschamps and Madre (1957, 1958) suggested that methotrimeprazine was of value in cases of melancholia and schizophrenia. Lambert *et al.* (1957) carried out a trial of the drug on 94 in-patients with various psychiatric disorders and found that its effects were similar to those of chlorpromazine, though it had a more marked sedative action. Sigwald *et al.* (1956) reached similar conclusions, adding that the effective dose of methotrimeprazine was rather lower than that of chlorpromazine. Baker and Thorpe (1958) selected 28 female schizophrenics showing deterioration who had relapsed after being given chlorpromazine. They too obtained results comparable to those of chlorpromazine. Substantially similar results have been obtained by Teulié *et al.* (1958), Baruk *et al.* (1958), Deshaies *et al.* (1958), Larue and Gosselin (1958), Collier and Martin (1958) and Gurtler *et al.* (1958). With the exception of the trial conducted by Baker and Thorpe, none of these studies was controlled.

METHOD

The present study was designed to compare the therapeutic effects of methotrimeprazine with those of a placebo and with chlorpromazine in chronic schizophrenia.

A total of 146 patients suffering from schizophrenia, 72 male and 74 female, were included in the trial. Selection was made on the basis of chronicity and lack of satisfactory response to previous treatment where this had been instituted. All the patients had been in hospital for at least one year and frequently for much longer than this. Of the patients interviewed, a number were excluded from the trial on the grounds of diagnostic uncertainty, severe deafness precluding adequate contact, or serious concomitant physical disease. The average age of the male patients—35 years with a range of 24 to 67 years—was less than that of the females—49 years with a range of 26 to 78 years.

Matching. Male and female patients were separately divided into three fairly comparable therapeutic groups A, B and C, based on age, length of stay in hospital and degree of deterioration. The latter was assessed using somewhat different criteria in the male and female groups. Amongst the male patients it was estimated largely on working capacity. Patients were placed into three categories: work grade 1—those who worked well without prompting; work grade 2—those whose work was satisfactory but required prompting; work grade 3—those who worked poorly or not at all. The female patients were also graded into three categories. In grade 1 there was fairly good personality preservation and retention of contact with the environment; in grade 2, personality changes were obvious with flattening of affect, withdrawal and loss of interest; and in grade 3, there was severe personality dilapidation with gross affective changes.

Table I overleaf shows the distribution of patients amongst the three therapeutic groups, together with their mean ages, mean durations in hospital and work or deterioration grades.

Previous Treatment

Some of the older patients who had been in hospital for many years had never had any special treatment. There were 22 such patients, 4 male and 18 female. The remainder had had standard forms of treatment in the past (see Table II). Although previous treatment was not considered as a criterion in matching the three groups, it so happened that from this point of view the distribution of the patients was fairly even.

TABLE I

Distribution of Patients in the 3 Therapeutic Groups According to Age, Length of Stay in Hospital and Work or Deterioration Grades

Male Patients

Group		No. of Patients	Mean Age (in years)	Mean Length of Stay in Hospital (in years)	Work Grade		
					1	2	3
Placebo (A)		25	36	6	11	8	6
Chlorpromazine (B)		23	37	6	8	10	5
Methotrimepazine (C)		24	33	7	8	11	5
Totals		72	35	6	27	29	16

Female Patients

Group		No. of Patients	Mean Age (in years)	Mean Length of Stay in Hospital (in years)	Deterioration Grade		
					1	2	3
Placebo (A)		25	48	11	7	7	11
Chlorpromazine (B)		25	50	15	7	7	11
Methotrimepazine (C)		24	49	15	5	7	12
Totals		74	49	14	19	21	34

TABLE II

Previous Treatment Received

Treatment Group				E.C.T.	Tran- quillizers	Deep Insulin	Leuco- tomy	None
Male								
Placebo	..	..	..	18	20	9	2	4
Chlorpromazine	..	..	..	21	22	8	2	0
Methotrimepazine			..	15	23	8	1	0
Total	..	..	..	54	65	25	5	4
Female								
Placebo	..	..	..	14	17	7	3	6
Chlorpromazine	..	..	..	14	15	5	2	6
Methotrimepazine			..	15	15	5	4	6
Total	..	..	..	43	47	17	9	18

(NOTE: Many patients have received more than one form of treatment.)

Effects of Withdrawal of Treatment Prior to the Trial

Eighty-seven patients (43 male and 44 female) were actually under treatment when selected for the trial, the great majority being on chlorpromazine or reserpine. In all these, therapy was suspended for a period of six weeks before the actual trial commenced. During this period, 8 (4 male and 4 female) improved, 41 (26 male and 15 female) became worse and 38 (13 male and 25 female) showed no change. One female paranoid schizophrenic, aged 59, who was originally selected for the trial became extremely disturbed and restless

when her daily 3 mg. of reserpine was stopped. She responded poorly to resumption of treatment and died a fortnight later. No post-mortem was done but for several months previously she had exhibited a persistent sinus bradycardia.

Administration and Dosage

Tablets identical in appearance were made up in stock tins for each patient. The active tablets each contained 50 mg. of chlorpromazine or methotrimeprazine. Only the pharmacist was aware of the identity of the tablets until the trial was over and he allocated the treatment to the three groups. Group A received placebo, group B chlorpromazine and group C methotrimeprazine. In all cases, treatment was commenced with one tablet twice daily. Patients were seen weekly and the dosage increased to 75, 100, 150, 200, 250 and 300 mg. in divided doses daily over a period of 7 weeks. The maximum daily dose (300 mg.) was continued for a further 2 weeks until the trial ended after 9 weeks.

During the period of the trial, patients remained in their original wards so that as far as possible environmental changes were minimized.

Assessment of Mental State

(a) *Clinical Evaluation.* All patients were interviewed on selection, and hereafter at weekly intervals. No attempt was made to standardize the interview. Notes were made on the mental state and any changes were recorded. At the end of the investigation, the clinical state of each patient was assessed on the following scale:

“Worse”—objective deterioration in the patient’s condition.

“No change”—absence of any apparent alteration in the psychosis.

“Slightly improved”—lessening in intensity of symptoms, with some improvement in overall behaviour but without any change in the basic psychotic pattern.

“Moderately improved”—substantial improvement in behaviour and rapport with marked lessening or disappearance of overt psychotic signs.

(b) *Nursing Staff Evaluation.* Nursing assessments were recorded on a behavioural rating chart adapted freely from the behavioural rating scale described by Baker and Thorpe (1956). Nine items were used as follows—general activity, dressing, talk, excretory habits, sociability, work, aggression, overt hallucinations and expressed delusions. Each item was graded on a 4 or 5 point scale and each point was given an arbitrary value of 1. The sisters, charge nurses and their deputies were instructed in the use of the scale and a separate item sheet was completed for each patient weekly. At the conclusion of the trial a score of +1 or -1 was given for each point representing improvement or deterioration. The sum of the scores for each item represented the direction of behavioural change during the course of the trial. It must be emphasized that figures have been used only for convenience. The steps indicated by the figures are unequal and no figure therefore can validly be compared with any other figure. The final results were recorded as “worse”, “no change” or “improved”.

RESULTS

The results are shown in Table III and a statistical analysis of these in Table IV. Examination of the combined figures reveals that the proportion of patients showing no change clinically is approximately the same in the three drug groups and is high, being 50 per cent. or over in all groups. This is in

TABLE III
Results—All Patients

Assessment	Drug	No Change	Slightly Improved	Moderately Improved	Worse	Total
Clinical	{ Placebo ..	28 (56)	6 (12)	2 (4)	14 (28)	50
	{ Chlorpromazine ..	28 (58)	8 (16)	7 (15)	5 (11)	48
	{ Methotrimeprazine ..	24 (50)	11 (23)	9 (19)	4 (8)	48
Nursing Staff	{ Placebo ..	7 (14)	24 (48)		19 (38)	50
	{ Chlorpromazine ..	9 (19)	26 (54)		13 (27)	48
	{ Methotrimeprazine ..	3 (6)	34 (71)		11 (23)	48

Results—Male Patients

Assessment	Drug	No Change	Slightly Improved	Moderately Improved	Worse	Total
Clinical	{ Placebo ..	11 (44)	6 (24)	1 (4)	7 (28)	25
	{ Chlorpromazine ..	11 (48)	3 (13)	5 (22)	4 (17)	23
	{ Methotrimeprazine ..	8 (33)	8 (33)	7 (30)	1 (4)	24
Nursing Staff	{ Placebo ..	3 (12)	14 (56)		8 (32)	25
	{ Chlorpromazine ..	5 (22)	12 (52)		6 (26)	23
	{ Methotrimeprazine ..	3 (13)	20 (83)		1 (4)	24

Results—Female Patients

Assessment	Drug	No Change	Slightly Improved	Moderately Improved	Worse	Total
Clinical	{ Placebo ..	17 (68)	0	1 (4)	7 (28)	25
	{ Chlorpromazine ..	17 (68)	5 (20)	2 (8)	1 (4)	25
	{ Methotrimeprazine ..	16 (67)	3 (13)	2 (8)	3 (12)	24
Nursing Staff	{ Placebo ..	4 (16)	10 (40)		11 (44)	25
	{ Chlorpromazine ..	4 (16)	14 (56)		7 (28)	25
	{ Methotrimeprazine ..	0	14 (58)		10 (42)	24

(Percentages in brackets)

TABLE IV
Statistical Analysis of Results

Assessment	Comparison*	χ^2	P (Df. = 2)	Significance
All Patients	Clinical	P $\times$ C	6.355	P < .05
		P $\times$ M	10.970	P < .01
		C $\times$ M	1.333	.5 < P < .7
	Nursing Staff	P $\times$ C	1.415	.3 < P < .5
		P $\times$ M	5.419	.05 < P < .1
		C $\times$ M	4.233	.1 < P < .2
Male Patients	Clinical	P $\times$ C	0.803	.5 < P < .7
		P $\times$ M	7.866	P < .02
		C $\times$ M	4.385	.1 < P < .2
	Nursing Staff	P $\times$ C	0.858	.5 < P < .7
		P $\times$ M	6.486	P < .05
		C $\times$ M	6.053	P < .05
Female Patients	Clinical	P $\times$ C	9.000	P < .02
		P $\times$ M	4.278	.1 < P < .2
		C $\times$ M	1.344	.5 < P < .7
	Nursing Staff	P $\times$ C	1.556	.3 < P < .3
		P $\times$ M	4.696	.05 < P < .1
		C $\times$ M	4.511	.1 < P < .2

* P=placebo: C=Chlorpromazine: M=Methotrimeprazine.

contrast to the nursing figures where the percentages showing no change are considerably lower (6-19 per cent.) with all three drugs.

The percentage of patients showing clinical improvement (combining the figures for "slight" and "moderate" improvement) is 16 per cent. with the placebo, 31 per cent. with chlorpromazine and 42 per cent. with methotrimeprazine, indicating a substantial difference between the placebo and the two "active" drugs. The advantage of chlorpromazine over the placebo is statistically significant ($p < 0.05$) and that of methotrimeprazine over placebo is highly significant ($p < 0.01$). Nursing staff assessment showed improvement with placebo in 48 per cent., with chlorpromazine in 54 per cent. and with methotrimeprazine in 71 per cent., thus showing the same trend, but statistically these results are not significant.

Of the male patients, 28 per cent. on the placebo, 35 per cent. on chlorpromazine and 63 per cent. of those on methotrimeprazine showed clinical improvement. Corresponding nursing assessment percentages indicate equal improvement scores with the placebo and chlorpromazine but a much greater response to methotrimeprazine, the figures being 56 per cent., 52 per cent. and 83 per cent. respectively. Both the clinical and nursing percentages for deterioration show that a considerably smaller proportion of patients deteriorated while on methotrimeprazine.

Among the female patients, clinical assessment showed an improvement rate in the placebo group of 4 per cent., with chlorpromazine of 28 per cent. and with methotrimeprazine of 21 per cent. The nursing assessment showed corresponding percentages of 40 per cent., 56 per cent. and 58 per cent.

Although the figures show trends suggesting that methotrimeprazine is somewhat superior to chlorpromazine, the differences are not significant statistically.

Side-Effects. No special arrangements were made to detect covert changes due to methotrimeprazine. Blood pressure recordings were not taken regularly and no blood counts were carried out. No reduction in dosage was made for elderly patients and all patients remained ambulant during the course of the trial. Side-effects were noted as they appeared and none was seen in the placebo group. Lethargy and drowsiness appeared in 6 male and 8 female patients on methotrimeprazine and in 3 male and 7 female patients on chlorpromazine. Dizziness was reported by one female patient on methotrimeprazine. Parkinsonian features occurred in 2 male and 3 female patients on methotrimeprazine. Only one male patient showed evidence of parkinsonism on chlorpromazine. The extra-pyramidal dysfunction was mild in each case and resolved on reduction of the dosage in the final week of the trial. There was one exception, a severely deteriorated catatonic female aged 43 years who developed severe parkinsonian rigidity with difficulty in swallowing during the last fortnight of the trial. The dosage of the methotrimeprazine was reduced without improvement and after a few days it was discontinued. Before any appreciable change could occur, she died suddenly. Post-mortem examination showed a bilateral bronchopneumonia with fibrofatty degeneration of the myocardium and fatty changes in the liver.

One paranoid middle-aged female patient on methotrimeprazine, in addition to drowsiness developed severe urinary incontinence which had not previously been a feature of her illness. No example of jaundice was seen during the trial. Baker and Thorpe (1958) noted leucopenia in one of their patients and a generalized erythematous rash occurred in another. One case of fatal agranulocytosis has been reported.

Relationship of the Number of Patients Clinically Improved, to Age, Length of Stay in Hospital and Working Capacity (Male) or Grade of Deterioration (Female). (See Table V)

TABLE V

Relationship of Number of Patients Clinically Improved to Age, Length of Stay in Hospital, Work Grade (Male) and Grade of Deterioration (Female)

(a) Relationship of Number of Patients Improved Clinically to Age

		Placebo		Chlorpromazine		Methotrimepazine	
Age		Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved
20-29	..	9	0	5	2	5	3
30-39	..	18	7	19	6	19	9
40-49	..	8	1	12	3	11	6
50-59	..	7	0	5	0	6	2
60-69	..	6	0	5	4	5	0
70-79	..	2	0	2	0	2	0
Total	..	50	8	48	15	48	20

(b) Relationship of Number of Patients Improved Clinically to Hospitalization

		Placebo		Chlorpromazine		Methotrimepazine	
Years in Hospital		Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved
0-9	..	40	7	28	10	31	15
10-19	..	4	1	11	4	10	4
20-29	..	3	0	8	0	4	1
30-39	..	3	0	1	1	3	0
Total	..	50	8	48	15	48	20

(c) Relationship of Number of Male Patients Improved Clinically to Work Grade

		Placebo		Chlorpromazine		Methotrimepazine	
Work Grade		Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved
1	..	11	4	8	2	8	7
2	..	8	3	10	4	11	5
3	..	6	0	5	2	5	3
Total	..	25	7	23	8	24	15

(d) Relationship of Number of Female Patients Improved Clinically to Grade of Deterioration

		Placebo		Chlorpromazine		Methotrimepazine	
Deterioration Grade		Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved
1	..	7	1	7	3	5	2
2	..	7	0	7	3	7	1
3	..	11	0	11	1	12	2
Total	..	25	1	25	7	24	5

(a) *Age*. It might be expected that the age of the patients would show a relationship to improvement and this is confirmed. There were 106 patients between the ages of 20 and 49 years and of these 37 (35 per cent.) showed improvement clinically compared with 6 patients out of 40 (15 per cent.) between the ages of 50 and 79 years. The effect of age was apparent in all three treatment groups.

(b) *Hospitalization*. Of 124 patients who had spent from 1 to 19 years in hospital, 41 (33 per cent.) showed improvement clinically. Of 22 patients who had been between 20 and 39 years in hospital, only 2 (9 per cent.) improved clinically.

(c) *Work Grade* (male patients). The figures for male patients show a direct relationship between clinical improvement and working capacity. Of 27 patients in grade 1, 13 (48 per cent.) improved. This compares with 12 out of 29 improved in grade 2 (41 per cent.) and 5 out of 16 improved in grade 3 (31 per cent.).

(d) *Grade of Deterioration* (female patients). The number of patients improved clinically bears an inverse relationship to the degree of deterioration. Of 19 patients in grade 1, 6 (32 per cent.) improved. In grade 2 there were 21 patients and 4 (19 per cent.) improved. In grade 3, out of 34 patients only 3 (9 per cent.) showed any improvement.

Relationship of Clinical Improvement to Alterations in Weight During the Trial

Of those patients who improved, 70 per cent. gained and 20 per cent. lost weight, the remaining 10 per cent. showing no weight change. Of the patients who showed no clinical change in their mental state, 54 per cent. gained weight, 31 per cent. lost weight and 15 per cent. remained the same. Thirty-nine per cent. of those who deteriorated gained weight compared with 48 per cent. who lost weight and 13 per cent. whose weight remained unaltered. Thirty-four patients showed an increase in weight with methotrimeprazine, 24 with chlorpromazine and 16 with the placebo.

Effects of the Drugs on Behaviour as Recorded on the Item Sheet by the Nursing Staff (see Table VI)

TABLE VI

Effect of the Drugs on Behaviour as Recorded by the Nursing Staff

Behaviour Item	Treatment Group	No Change	Improved	Worse	Total
Activity	Placebo	35	7	8	50
	Chlorpromazine ..	33	8	7	48
	Methotrimeprazine	31	11	6	48
Dressing	Placebo	37	6	7	50
	Chlorpromazine ..	39	3	6	48
	Methotrimeprazine	34	7	7	48
Talk ..	Placebo	34	8	8	50
	Chlorpromazine ..	36	11	1	48
	Methotrimeprazine	26	16	6	48
Habits	Placebo	42	6	2	50
	Chlorpromazine ..	40	5	3	48
	Methotrimeprazine	38	6	4	48

TABLE VI—*continued*

Behaviour Item	Treatment Group	No Change	Improved	Worse	Total
Sociability ..	Placebo	36	5	8	50
	Chlorpromazine ..	35	8	5	48
	Methotrimeprazine	37	9	2	48
Work ..	Placebo	31	10	9	50
	Chlorpromazine ..	35	7	6	48
	Methotrimeprazine	27	12	8	48
Aggression ..	Placebo	37	8	5	50
	Chlorpromazine ..	23	23	2	48
	Methotrimeprazine	22	24	2	48
Hallucinations	Placebo	33	8	9	50
	Chlorpromazine ..	25	12	11	48
	Methotrimeprazine	30	13	5	48
Delusions ..	Placebo	31	12	7	50
	Chlorpromazine ..	30	13	5	48
	Methotrimeprazine	26	14	8	48

“Activity” shows a slight advantage of methotrimeprazine over the placebo and chlorpromazine.

“Talk”—the numbers improved are substantially greater with methotrimeprazine and this is true also for improvement in “sociability”. Both chlorpromazine and methotrimeprazine influenced “aggression” favourably in a much greater number of patients than the placebo. The effect on “hallucinations” also suggests some superiority for both the active drugs over the placebo. In the case of “dressing”, “excretory habits”, “work” and “delusions”, there was no advantage shown for the chlorpromazine and methotrimeprazine over the placebo.

DISCUSSION

Early assessment of the effects of new drugs in psychiatric practice is of fundamental importance and this can only be done with any degree of accuracy by controlled therapeutic trials. Foulds (1958) in his survey of the Anglo-American literature noted that success in treatment was claimed in only 19 per cent. of controlled studies as compared with 85 per cent. of uncontrolled trials. Marley (1959) referring to the work of Wolf (1950), Beecher (1955) and Tibbets and Hawkings (1956) comments that a 15–58 per cent. favourable response may follow administration of a placebo.

Many writers have indicated the problems and difficulties which such trials raise, not the least of which is their time-consuming nature, as Hargreaves *et al.* (1957) have pointed out. Moore and Martin (1957) observed that controlled blind investigations, satisfactory to statisticians, are difficult to arrange with drugs which have obvious side-effects; and in illnesses such as schizophrenia, the natural history of which is in any case fluctuating and subject to remission, the results may be influenced by the increased attention paid to the patients by the staff.

In this study, all the patients were chronically disabled, many to a very severe degree. It was originally intended that they should be classified into hebephrenic, catatonic and paranoid sub-groups. Many of the patients were so disorganized that it was impossible to type them with any degree of accuracy

and it was felt that any results based on such a classification would serve little or no useful purpose.

It is necessary to consider possible reasons for the disparity in the results of the clinical as compared with the nursing assessments. The numbers of patients recorded as showing "no change" in all three therapeutic groups are much smaller when assessed by the nursing staff than by the medical staff. On the other hand, in all other groups—"worse" as well as "improved"—the percentages are higher when assessed by the nurses. This may be an expression of the fact that nurses are in closer and more constant contact with the patients and in a position to observe and note minor changes of behaviour which would not be revealed in the interview situation. Alternatively they might indicate that the nurses are more impressionable than the medical staff and are less content to accept a negative result. This view is supported particularly by the high incidence of improvement recorded by nurses in the placebo group.

Doubt may be felt about the reliability of "global" clinical assessments of the mental state, whether carried out by nursing or medical staff. Marley (1959) in his recent paper contrasts the subjective and objective assessment of the effects of drugs and considers that the ideal would be to combine as many subjective and objective criteria as expedient. He adds that "quantification" of drug response by arbitrary rating rather than clinical assessment may be helpful, but quotes Lorr (1954), who comments that "attempts to refine clinical judgment with rating scales and check lists have not proved the superiority of such measures".

The results of this trial show that both chlorpromazine and methotrimeprazine are more effective in chronic schizophrenia than a placebo. The figures are rather more impressive in the case of male than female patients. This may well reflect differences in age, length of hospitalization and degree of deterioration. As a group, the male patients were younger, their stay in hospital shorter and their degree of deterioration less. It is clear that neither chlorpromazine nor methotrimeprazine is a panacea for the long-stay deteriorated schizophrenic and in no case could the improvement be described as more than moderate in degree. It is likely that many of the patients included in this trial have passed beyond the reach of pharmacological remedies and must be regarded as permanently crippled mentally.

In this trial only one level of dosage was employed and this was the same for chlorpromazine and methotrimeprazine. It is likely that in practice the optimum dose would vary from case to case and the therapeutic response might be altered. Although methotrimeprazine appears to be well tolerated when taken by mouth, and elderly patients did not seem to be particularly prone to side-effects, parkinsonism was more frequent than with chlorpromazine and its incidence may be related to the dosage employed. Sigwald *et al.* (1956) and Lambert *et al.* (1957) found that a smaller dose of methotrimeprazine is required than with chlorpromazine and the ratio they both suggest is 2 to 3 (i.e. 30 mg. methotrimeprazine is equivalent to 45 mg. chlorpromazine).

A point of some importance emerged shortly after the original selection of the patients. Following withdrawal of drugs and of maintenance E.C.T., 47 per cent. of the patients who had been receiving treatment showed deterioration in behaviour. This tended to produce anxiety in the nursing staff concerned and was particularly disturbing where many such patients were in the same ward. In these circumstances the support and encouragement of the medical staff is necessary and very helpful. Education of all grades of nursing staff in the methods and aims of therapeutic trials is an essential prerequisite to their success.

SUMMARY

A double-blind controlled investigation of a new phenothiazine derivative—methotrimepazine (Veractil)—in a group of 146 male and female chronic schizophrenic patients is described. The trial was designed to compare the effects of the drug with those of chlorpromazine and with a placebo. As a group, the female patients were older, had been longer in hospital and were more deteriorated. The male patients generally were more actively psychotic but less deteriorated and their average age and length of stay in hospital was less than the female.

Methotrimepazine in the dosage employed was found to be a potent drug and to be at least as effective as chlorpromazine. Parkinsonism and drowsiness were more frequently encountered with methotrimepazine and one female patient who subsequently died was severely affected. Disparity in the results of clinical and nursing assessments are described and discussed.

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EXTREME RESPONSE SET, DRIVE LEVEL AND ABNORMALITY IN QUESTIONNAIRE RIGIDITY*

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INTRODUCTION

In several recent experiments involving motor performance (1), learning (7), immediate recall (2), expressive movement (5) and confidence in performance (3), significant relationships with a questionnaire measure of rigidity have been obtained. In view of the fact that despite a considerable amount of work no general trait of rigidity has hitherto been recognized, it was decided to clarify the reasons for the above results. Two steps are undertaken. The first step, published separately, is concerned with a systematic analysis of the experimental variables which yielded significant correlations with rigidity. In a series of investigations, the attempt is made to discover the experimental conditions necessary for a significant interaction of rigidity with test responses to occur.

The second step deals with an analysis of questionnaire criteria of rigidity, as undertaken in the present study. Even in the questionnaire field rigidity has received little recognition as a general factor. More recently, results have been obtained which strongly point to the existence of such a factor which appears essentially independent of other dimensions like extraversion and neuroticism. Nigniewitzky (15, 16), using a representative French sample, found scales of rigidity, dogmatism, intolerance of ambiguity and of fascism to have high loadings on a factor termed rigidity. A cross-validation of this result is described in the present paper. The F-scale was omitted because of its specific prejudice content. With slight modifications, all other rigidity scales were used as in Nigniewitzky's original studies.

The determination of the generality of a factor of rigidity represents one task of the present experiment. A second aspect is devoted to an analysis of the specificity of the same factor. Rigidity is thought of as a complex of various modes of behaviour, the analysis of which may provide differential information. The rigidity factor of Nigniewitzky appears, for example, to be composed of characteristics like extreme response set, striving for unrealistic or unreasonable goals, high prejudice, obsessionality, high intensity of motivation, and so forth. Apart from these features, our own empirical findings (6) have shown that the Nigniewitzky rigidity scale discriminates reliably between normals and abnormals. Abnormality of response may thus form a further aspect of rigidity.

Another suggestion was derived from a recent experiment in which abnormal and personality correlates of desire for certainty were studied (3). Of the various personality criteria used, a scale of rigidity was found to correlate highest with certainty, usually considered a motivational variable. Furthermore, rigidity appeared to give rise to curvilinear relationships with certainty when

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measured under suitable conditions. From this the suggestion may be derived that drive of one form or other is a property of rigidity.

These considerations suggest considerable complexity of the rigidity factor. Further discriminable aspects of rigidity could no doubt be found, and it is possible that the neglect of their analysis has contributed significantly to the existing disagreement in experimental results. The present investigation, therefore, deals with specific validity by including fairly heterogeneous questionnaires characteristic of several of the aspects mentioned. The main aspects chosen are extreme response set, drive level and abnormality.

Specificity of rigidity may be investigated not only by analysing various aspects of the factor as a whole but also by emphasizing the differences between the sub-scales. For this reason, item analyses of the four rigidity scales were carried out in order to increase the scale specific validities of the individual items.

Most of the scales used in the present study, with the exception of E, N and MAS which have been published by the respective authors, are appended in their item-analysed form.

Rigidity factor	{	NR: rigidity (15, 16)
		CPIR: California Psychological Inventory of Rigidity (12)
		Do: dogmatism (17)
		IA: intolerance of ambiguity (15)
		Dr: drive (new construction)
PFCL +2: personal friend check list, extreme positive response set (derived from Soueif, 21)		
E: extraversion (9)		
N: neuroticism (9)		
MAS: manifest anxiety (22)		

The scales which contributed outstandingly to the rigidity factor of Nigniewitzky were NR, CIPR, Do and IA. They are summarily referred to as "rigidity".

The Personal Friend Check List requires the subject to respond in degrees (+2, +1, 0, -1, -2) to 100 adjectives. While the item content is believed to be of relatively little importance, the main feature of this check list is the extremeness of response. Of the two extreme response types, only the number of positive extreme responses is used as a score for reasons indicated elsewhere (6). Significant correlations between rigidity and this score have been obtained on previous occasions (6).

MAS is included because it has been used as both an indicator of abnormal symptomatology and of drive strength (Inglis, 13; Jones, 14).

For similar reasons, N is employed to assess the abnormality and the drive aspect of rigidity. Although Eysenck has not elaborated a drive theory of his own, Inglis (13) has taken up a suggestion made by the former investigator (Eysenck, 10) and has accepted N and E in combination as indicators of drive strength. According to this view, drive strength increases along the composite continuum: neurotic extraverts—stable extraverts—stable introverts—neurotic introverts. A test of this theory will be attempted.

It is realized that all questionnaires quoted so far, with the exception of E, have a strong abnormal connotation in the sense that they discriminate reliably and significantly between normals and abnormals. Nevertheless, they have frequently been assigned a most important task as criteria of drive strength. Apart from this obvious complexity, the scales quoted do not express drive

verbally, with the exception of some of the rigidity items. In the instance of E, N and MAS drive is almost entirely inferred.

For these reasons a new drive scale (Dr) is constructed, the items of which express drive directly and in a manner which is hoped to prevent significant differentiation between normals and abnormals. This "manner" of construction is difficult to define, but the author intended to formulate statements expressing strong motivation and avoiding, at the same time, the connotations of lack of realism, prejudice and/or unreasonableness, as frequently found in the rigidity variables. Thus it was hoped to assess the intensity typical of a portion of the rigidity items while removing the effects of abnormality of response.

AIMS AND PREDICTIONS

As this study serves a number of purposes, aims and predictions may be briefly enumerated. The aims are as follows: to cross-validate the factor of rigidity, obtained by Nigniewitzky in France, using English samples; to establish the degree of correlational dependence of this factor on the personality dimensions of extraversion and neuroticism; to determine the relationships of extreme positive response set to the factors mentioned; to determine the differentiation between normals and abnormals of rigidity and related scales; to secure predictions for differences of the same kind between some abnormal categories and to assess the effects of irrelevant factors of occupational status and age.

The expectations, largely derived from the studies already mentioned, are as follows. With the exception of N and MAS, both of which are measures of neurotic tendencies, highest intercorrelations are between the rigidity variables. N, MAS and PFCL +2 correlate moderately or lowly with rigidity. E correlates insignificantly and, if anything, negatively with rigidity. Abnormals score significantly higher on all rigidity and related variables, with the possible exception of Dr. In general, predictions are less easily made for Dr, an entirely new scale. If the assumption is correct that rigidity, a.o., measures "unreasonable" and "abnormal" kind of motivation, whereas Dr expresses "reasonable" and "normal" drive, the following may be expected. The correlation between Dr and rigidity will be low, but possibly significant because of common drive elements. Dr will not correlate significantly with abnormal tendencies (N and MAS). The significance of differentiation between normals and abnormals will diminish in the order: neuroticism (N and MAS), rigidity (NR, CPIR, Do and IA), PFCL +2 and Dr. The latter variable should produce insignificant differences.

METHOD

1. *Questionnaires and scoring.* The questionnaires used have already been named in the introduction.

For MAS the number of items answered in the anxiety direction is used as score. As regards the PFCL, only the positive extreme response, or Extr. +2, is analysed at present. The number of +2s serves as score. For all remaining scales, two points are awarded for a response in the direction indicated by the scale name and one point for an undecided response, or response to a question-mark.

2. *Subjects.* Eighty-eight normal and 105 abnormal persons were tested with all questionnaires, except for MAS in the case of the normals. As occupational status has been demonstrated to interact significantly with a number of the scores used (Brenghelmann, 4), subjects are divided into four

sub-categories, as follows: I=unskilled occupations (untrained labourers, factory workers, shop assistants, etc.); II=skilled occupations (clerks, typists, trained craftsmen, technicians, etc.); III=higher trained and/or independent occupations (executives, independent business people, officers of forces, higher officials, etc.); and IV=academic professions. The frequencies for these sub-groups distribute as shown in Table I.

TABLE I
Distribution of Subjects to Four Occupational Categories

Occupational status	..	I Unskilled	II Skilled	III Higher- trained	IV Academic	Total
Controls (all males)	..	17	35	15	21	88
Abnormals	Males ..	20	20	22	4	66
	Females ..	18	16	0	5	39
	Total ..	38	36	22	9	105

As may be seen, occupational status is in the average lower for the patients than for the controls. When tested for significance, a chi-square of 12.75 (3 d.f.) is obtained, which is significant at the 1 per cent. level. This factor, therefore, requires consideration in the assessment of differences between normals and abnormals.

Clinical diagnosis may play an important part. A corresponding frequency distribution of the patients is given in Table II.

TABLE II
Number of Subjects in Clinical Categories

Number of Subjects						Males	Females	Total
Dysthymics	..	..	..	..	..	19	15	34
Hysterics	..	..	..	..	..	16	11	27
Schizophrenics	..	..	..	..	..	8	2	10
Depressions (psychotic)	..	..	..	..	..	3	6	9
Inadequate personalities	..	..	..	..	..	7	0	7
Schizoid personalities	..	..	..	..	..	3	1	4
Addicts (drugs or alcohol)	..	..	..	..	..	4	1	5
Others (unclassifiable)	..	..	..	..	..	6	3	9
Total	..	..	..	..	..	66	39	105

As to type of patients, no attempt for selection was made except that patients were volunteers and that testing was arranged in hospitals predominantly occupied by neurotics and less severe cases of psychotics. As a rule, the psychotics used in the present study were either well on their way to recovery or sufficiently recovered to be discharged. The chronicity of disease varied to a considerable degree. This factor was not assessed. Finally, only such patients were selected who did not receive any physical treatment save for ordinary night sedation. If physical treatment had been completed a period of four weeks was allowed to pass before patient was tested.

Age requires consideration because of its positive relationship to rigidity. In the present study the mean age was 37.24 (S.D.=12.01) for the normals and 35.85 (S.D.=11.25) for the abnormals. As assessed by a t-test analysis

($t=0.64$, with 191 d.f.), this difference is insignificant. For the overall differentiation between normals and abnormals age is therefore unlikely to play an important part.

3. *Item analysis.* As neither the Dr nor the four rigidity scales had been systematically analysed using samples drawn from the British culture, a double item analysis within and between these scales was carried out. The normal group, which was tested first, was used for this analysis. In the first analysis, those items were selected which correlated significantly with the respective scales but not so with any of the other scales. The analysis was then repeated with items found to be the best differentiators. The criteria of item acceptance were significant differentiation between the high and low scoring halves, using the 5 per cent. level of significance; linear relationship through the quartiles of the entire sample, and a response frequency with a minimum of 20 or a maximum of 80 per cent. The item analysed versions of the questionnaires were subsequently administered to the abnormals for comparison with the normals in terms of intercorrelations, effects of occupational status and differentiation.

RESULTS

1. *Item analysis.* As a result of the first analysis, the NR and Do scales lost a considerable number of their original items, partly because of insignificant correlation with the respective total scores and partly because of too great complexity (significant correlation with several other scales). The original and final numbers of items employed in the various scales are shown in Table III. A systematic item analysis of the PFCL has not yet been carried out.

TABLE III

Number of Items Pertaining to the Various Questionnaires

Number of Items in Scales							Before Item-analysis	After Item-analysis
NR ..	..	..	..	..	..	..	28	14
CPIR	..	..	..	..	..	..	14	15
Do ..	..	..	..	..	..	..	36	16
IA ..	..	..	..	..	..	..	20	17
Dr ..	..	..	..	..	..	..	17	14
E ..	..	..	..	..	..	..	24	*
N ..	..	..	..	..	..	..	24	*
MAS	..	..	..	..	..	..	50	*

* Not item-analysed.

The item specificity of the analysed scales varies as follows. None of the items of NR, Do and Dr correlated significantly with any of the scales but their own, while the internal correlations with their own scales were significant at the 1 per cent. level for all items. Of CPIR and IA a number of items correlated significantly with other scales, but not higher than at the 2 per cent. level. Of CPIR, items 1, 7 and 10 correlated significantly with NR; 4 and 9 with Do; and 4, 10 and 11 with IA. Of IA, items 6, 13 and 14 correlated significantly with NR; 1, 5, 7, 8 and 10 with Do; and 13 with IA. In several instances items were exchanged between the scales.

As seen from Table IV, the overall size of intercorrelations was hardly affected by the item analysis. However, a considerable reduction in the range of coefficients occurred for all significantly intercorrelating scales (rigidity and

related scales plus N). High coefficients decreased and low coefficients increased in size. The former effect may be due to the weeding out of items which correlated significantly with several scales. The latter effect may be due to the selection of scale specific (significant) items, resulting in the measurement of a "purer" factor of rigidity.

Distributions of scores are shown in Figure 1, separately for normals and abnormals.

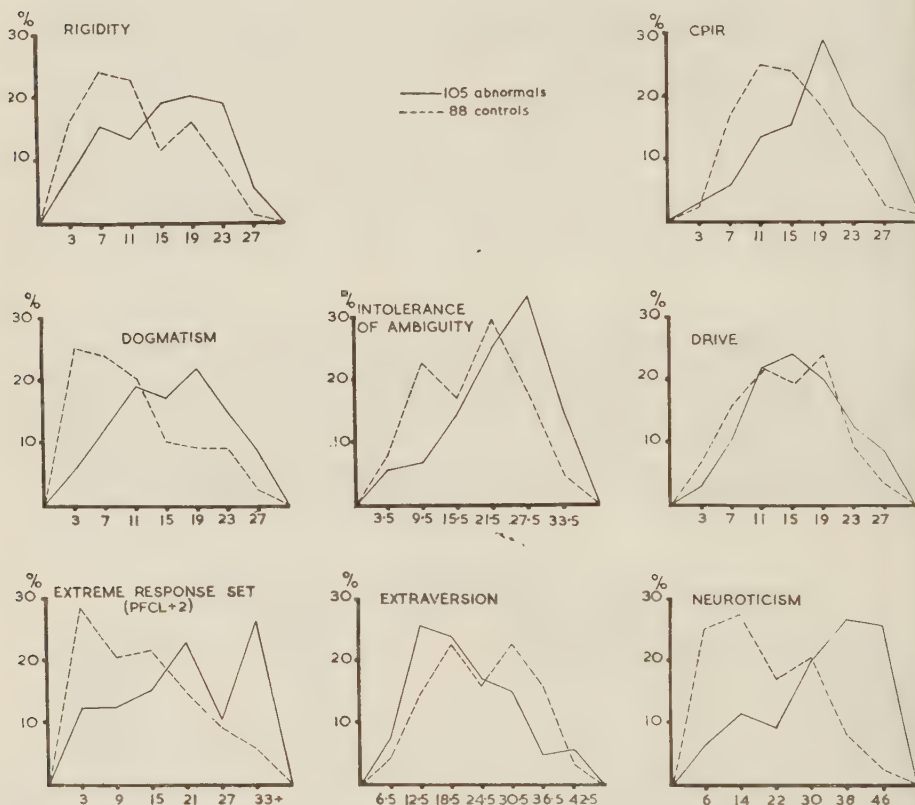


FIG. 1.—Score distributions for all scales used in both the normal and the abnormal sample. (MAS not used with the normals.)

The normal/abnormal dichotomy leads to considerable differences in distribution for all scales but Dr. This result is discussed in a later section.

2. *Correlational analysis.* All pairs of variables were inspected for linearity. No obviously non-linear relationships were observed. The coefficients of intercorrelation are given in Table IV, separately for normals (original scores), normals (item-analysed scores) and abnormals (item-analysed scores).

A number of conclusions may be drawn from these fairly clear-cut results, the inspection of which is facilitated by the arithmetically computed mean coefficients, shown in Table V.

The uniformly high correlations between NR, CPIR, Do and IA confirm the existence of a general factor of rigidity, obtained by Nigniewitzky on a French sample.

The drive scale correlates significantly with rigidity, thus confirming the

TABLE IV

Questionnaire Intercorrelations

Upper Figures in each Cell: 88 Normals (original scores); Centre Figures: Same Normals (item analysed scores); Lower Figures: 105 Abnormals (item analysed scores). MAS used with Abnormals only. PFCL +2, E, N and MAS not Item Analysed

TABLE 10. Comparison of the results of the 11-22, 22, 11 and 11-22										
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Levels of significance: * = 5 per cent.; † = 1 per cent.

Validity: Correlations between original and item analysed scales

TABLE V

Correlations of Various Factors with the Rigidity Complex

	88 Controls	105 Abnormals
1. Mean intercorrelations of the rigidity complex (NR, CPIR, Do and IA)	..	..
2. Drive vs. 1 ..	0.48	0.55
3. PFCL +2 vs. 1 ..	0.27	0.40
4. Neuroticism vs. 1 ..	0.29	0.28
5. Manifest anxiety vs. 1 ..	0.42	0.24
6. Extraversion vs. 1 ..	—	0.28
7. Age vs. 1 ..	-0.14	-0.10
	0.23	0.20

hypothesis that rigidity scales, apart from other characteristics, have drive property. The fact that Dr correlates lower with rigidity than the rigidity variables amongst each other may indicate that the former factor is, as intended, related to a specific aspect of the relatively heterogeneous complex of rigidity. The specificity of this relationship is further demonstrated by the finding that all correlations but one between Dr and the remaining variables (N, MAS, E and age) are insignificant.

Extreme positive response set is significantly correlated with rigidity, indicating a high degree of (positive) response intensity in the rigid personality. This result has now been obtained on a number of occasions and may be considered an established fact.

The neuroticism variables (N and MAS) also correlate significantly with rigidity. This finding disagrees with Nigniewitzky's result of an insignificant relationship.

Extraversion correlates insignificantly with rigidity. The fairly high negative correlation with N and MAS in abnormals, in contrast to a corresponding insignificant coefficient in the normal group, agrees with frequent previous results obtained by various authors.

The significant relationship between rigidity and age is as expected.

3. *Differentiation between normals and abnormals.* A t-test analysis between normals and abnormals is shown in Table VI, separately for males and females.

TABLE VI

Statistical Assessment of Differences Between Normals and Abnormals. MAS not Tested in the Control Sample

	(1) 88 Male Controls		(2) 66 Male Abnormals		(3) 39 Female Abnormals		t-ratio		
	$\bar{x}$	SD	$\bar{x}$	SD	$\bar{x}$	SD	1 vs. 2 152 d.f.	1 vs. 3 125 d.f.	2 vs. 3 103 d.f.
NR ..	11.44	6.62	14.92	6.33	15.43	7.47	3.29†	3.01†	0.37
CPIR ..	14.52	6.00	17.92	6.34	19.00	6.18	3.40†	3.85†	0.85
Do ..	10.28	6.97	14.30	6.41	17.92	6.41	4.42†	5.84†	2.80†
IA ..	16.43	7.97	20.21	7.53	22.51	7.96	2.98†	3.97†	1.48
Dr ..	14.15	6.11	15.30	6.19	16.00	6.07	1.15	1.58	0.56
PFCL+2	12.93	9.38	20.29	13.02	22.54	13.24	4.08†	4.67†	0.85
E ..	23.61	9.12	20.96	8.17	19.82	11.40	1.87	2.00*	0.59
N ..	17.99	10.82	29.18	12.79	33.26	10.81	5.88†	7.34†	1.67
MAS ..	—	—	24.97	11.63	28.15	10.33	—	—	1.41
Age ..	37.24	12.01	34.27	10.99	33.92	11.81	1.68	1.57	0.15

Significance levels: * = 5 per cent.; † = 1 per cent.; ‡ = 0.1 per cent.

MAS was not employed in the control group.

Results are generally as expected. Neuroticism differentiates very sensitively between normals and abnormals, and the latter group shows a significant tendency to be more introverted.

The outstanding main finding is that all rigidity variables (NR, CPIR, Do and IA) discriminate at a high level of significance. The same applies to extreme positive response set (PFCL +2).

A further outstanding characteristic is the insignificance of the difference with regard to drive. This result may be taken to support the view that Dr is a measure of "normal" drive.

With the exception of Do, no appreciable differences are obtained between male and female abnormals.

4. *Effects of occupational status.* On a previous occasion, using the German translation of the present questionnaires on 200 German nationals, significant differences between status categories of the kind employed in the present study were found for Do, IA and PFCL +2 (Bengelmann, 4). As normals and abnormals were significantly different with respect to occupational level (Table I) this factor is assessed in the following analysis. Firstly, means and standard deviations were computed separately for the four occupational categories, results being shown in Table VII.

With one exception (NR, category IV), means are consistently higher for the abnormal sub-groups on all variables, which discriminated significantly between normals and abnormals. This indicates that the quality of response is similar regardless of occupational level. The relative, or quantitative differences between the occupational categories are assessed by means of analysis of variance. Analyses were carried out separately for normals and abnormals and the results are given in Table VIII.

TABLE VII

Means and Standard Deviations of Four Occupational Categories. MAS not Tested in the Normal Sample

		Occupational Status							
		I Unskilled		II Skilled		III Higher-trained		IV Academic	
		17 C	38 E	35 C	36 E	15 C	22 E	21 C	9 E
NR	$\bar{X}$	10.71	15.76	12.29	16.53	11.40	14.86	10.67	7.33
	SD	7.45	6.14	7.58	6.58	5.07	6.55	5.38	5.92
CPIR	$\bar{X}$	15.06	19.32	14.80	18.81	15.33	17.50	13.05	14.22
	SD	7.52	6.11	5.65	5.81	5.47	5.62	5.75	9.04
Do	$\bar{X}$	11.29	17.29	10.74	15.64	10.07	13.18	8.86	14.78
	SD	9.16	7.13	6.75	6.61	5.86	5.34	6.25	6.12
IA	$\bar{X}$	16.59	22.42	18.06	21.50	17.33	20.32	12.95	15.44
	SD	7.96	7.03	7.84	7.77	7.73	8.24	7.81	7.75
Dr	$\bar{X}$	14.18	16.32	14.14	16.56	12.80	14.18	15.10	13.00
	SD	6.25	6.40	5.54	5.79	6.57	6.56	6.81	4.70
PFCL +2	$\bar{X}$	15.88	24.26	13.00	20.58	10.73	18.86	11.86	16.67
	SD	12.07	13.50	9.08	13.95	11.11	10.84	8.56	4.47
E	$\bar{X}$	26.35	20.84	21.57	20.28	23.73	20.00	24.71	21.56
	SD	7.59	9.35	9.27	10.29	10.05	8.32	9.16	10.66
N	$\bar{X}$	21.59	32.61	17.26	29.33	18.13	30.18	22.67	29.33
	SD	12.24	11.01	10.69	13.06	12.04	11.84	8.82	4.81
MAS	$\bar{X}$	—	27.97	—	25.69	—	25.27	—	22.44
	SD	—	10.29	—	12.20	—	10.67	—	12.72

C=controls, E=experimental, abnormal sub-groups.

TABLE VIII

Analysis of Variance Between Occupational Categories

F-ratio		88 Normals (3/84 d.f.)	Significance	105 Abnormals (3/101 d.f.)	Significance
NR		*	—	5.22	1%
CPIR		*	—	1.84	N.S.
Do		*	—	1.89	N.S.
IA		1.95	N.S.	2.14	N.S.
Dr		*	—	1.25	N.S.
PFCL +2		*	—	1.28	N.S.
E ..		1.21	N.S.	*	—
N ..		*	—	*	—
MAS		Not tested	—	*	—

* =within group variance larger than between group variance.

N.S.=not significant.

These findings are practically clear-cut. Significant differentiation between the occupational levels is found in one instance only (NR, abnormals). This single result may be considered to have occurred by chance, firstly, because the remaining rigidity scores did not differentiate significantly and, secondly, because in the previous study on Germans already mentioned (4), NR did not provide significant differentiation. It is concluded that occupation does not contribute significantly to rigidity as far as the present conditions are concerned.

5. *The role of hysteria/dysthymia.* In the light of the excellent discrimination between normals and abnormals, an analysis between abnormal categories would be of particular importance. Because of the small sub-samples (Table II) this analysis is at present restricted to the dichotomy hysteria/dysthymia, as

defined by Eysenck (11). According to this author hysterics and dysthymics are differentiated significantly along the E-dimension, not however along the N-dimension. As the rigidity variables correlate significantly with N only it may be expected that no significant relationship with the dichotomy in question is obtained. This is in fact borne out by the results shown in Table IX.

TABLE IX
Differences Between the Neurotic Dichotomy Hysteria-Dysthymia

			Hysterics	Dysthymics	t-ratio	Significance (59 d.f.)
NR	..	$\bar{X}$	16.00	15.79	0.12	N.S.
		SD	6.56	7.25		
CPIR	..	$\bar{X}$	18.59	19.18	0.37	N.S.
		SD	5.81	6.39		
Do	..	$\bar{X}$	16.67	16.68	0.01	N.S.
		SD	5.38	7.89		
IA	..	$\bar{X}$	22.11	22.15	0.03	N.S.
		SD	6.89	8.80		
Dr	..	$\bar{X}$	15.30	16.12	0.50	N.S.
		SD	6.81	6.02		
PFCL +2	..	$\bar{X}$	16.48	21.82	1.65	N.S.
		SD	9.85	14.32		
E	..	$\bar{X}$	24.52	17.58	2.72	1%
		SD	8.91	10.66		
N	..	$\bar{X}$	31.48	32.65	0.40	N.S.
		SD	11.49	11.42		
MAS	..	$\bar{X}$	25.33	29.06	1.47	N.S.
		SD	8.86	10.43		

Firstly, it is seen that the hysterics are significantly more extraverted than the dysthymics. Previously such result has been achieved when comparing psychopaths with dysthymics, not however between dysthymics and hysterics proper. The same applies to the present study where more than 80 per cent. of the "hysterics" were psychopaths.

The term "psychopath" was applied to patients categorized by clinicians as personality disorder, character disorder, or psychopathy. Schizoid and inadequate personality disorders were treated as separate categories.

As required, hysterics and dysthymics are not significantly differentiated by means of N. None of the remaining scores differentiates significantly between the two groups in question, indicating that rigidity and related variables are unspecific in this respect. Like neuroticism, they vary in the direction of general abnormality.

6. *Extraversion and neuroticism as a combined indicator of drive.* In the introduction the theory of Inglis (13) was quoted that drive intensity increases as a combined function of E and N in the order: neurotic extraverts (NE)—stable extraverts (SE)—stable introverts (SI)—neurotic introverts (NI). This theory requires a non-linear relationship of drive with neuroticism and a linear relationship with extraversion. As long as rigidity and Dr possess drive property of one kind or other, the above hypothesis is contradicted by the results shown in the correlation matrix (Table IV), all variables of which are linearly inter-related. As neuroticism correlates significantly with rigidity both NE and NI score higher on this factor than SE and SI, thus causing the hypothesized drive

continuum to assume non-linearity. For Dr, the "normal" drive scale, a linear relationship is possible. Because of its tendency to correlate positively with E, the ascent of the gradient would be opposite to prediction. All scores were actually inspected from the point of view discussed, but no support was found for the theory of Inglis.

DISCUSSION

Highly significant intercorrelations between two measures of rigidity and one each of dogmatism and intolerance of ambiguity have confirmed Nigniewitzky's finding of a general factor of rigidity, obtained in France. This result agrees well with two similar analyses carried out on German normal samples differing in occupational composition (4). Further agreement is derived from the study of Rokeach and Fruchter (19), who used scales very similar to those of Nigniewitzky. In this study a factor of rigidity was extracted on which dogmatism and authoritarianism had high loadings.

The finding that the latter variables had also positive loadings on a factor of anxiety agrees with the present result of a positive correlation between the rigidity variables on the one hand and neuroticism and manifest anxiety on the other. However, as neither the French nor the German samples gave rise to similar results the theory by Rokeach and Fruchter that "ideological dogmatism has its major motivational basis in anxiety" must be treated with reserve.

The main emphasis of Rokeach and Fruchter was not, however, as much on communality as on specificity. The authors took pains to point to differences between questionnaire criteria with high loadings on the same factor. Some such differences between dogmatism and rigidity were described. Furthermore, in a previous experiment, Rokeach, McGovney and Denny (18) have shown that differences of a qualitative kind may be attached to dogmatism and rigidity despite their high intercorrelation. Thus by analysing for specific rather than common effects important information may be gained.

A very similar point of view was adopted for the present experiment by employing questionnaires with the aim to validate differential aspects of rigidity. The significant but relatively low correlations with PFCL +2, Dr and neuroticism (N/MAS) suggest the possibility of isolating various aspects of rigidity postulated to be a rather complex factor. Experimental validation separately for these differential aspects may then be carried out.

Of the specific results the Dr scale has been particularly useful. As stated in the introduction the scale was constructed to represent a "normal", "reasonable" kind of motivation. This aim was achieved as demonstrated by lack of significant differentiation between normals and abnormals. Abnormals, therefore, do not judge themselves to be more motivated than normals as far as realistic striving is concerned. However, they mobilize an excessive degree of energy in stating their attitudes and in aiming for unrealistic, ambiguous and/or unreasonable goals. The consistently significant correlation between Dr and rigidity confirms the view that desire for motivation is part of the rigidity complex. The remaining scales of N, MAS and E correlate, with one exception (N in normal group), insignificantly with Dr. From this it is concluded that these criteria do not possess drive characteristics as measured by the present scale.

It may now be asserted that amongst other qualities the rigidity complex is characterized by desire for drive, extremeness of response and probably a fairly general intensity of set. This description is reminiscent of Duffy's (8)

syndrome of "energy mobilization" or "energy level", which covers such frequently used terms as "instincts", "drives", "urges", "tensions", "motives", or "libido". Energy mobilization may form the basis to rigidity. Following Duffy, it may then be contrasted with her second basic behavioural concept of "goal-direction". This deals with the form or direction of behaviour, while variables of the energy type are concerned with variations in the strength with which such behaviour is conducted. With a view on abnormality it may be added that economy in mobilization and adequacy in regulation of psychological energies represent important additional problems.

As abnormals score high on ("abnormal") rigidity, not however on ("normal") Dr, it may be said that they mobilize and use excessive energy in an uneconomic and inadequate manner. The question is now asked which type of psychiatric category or syndrome is typical of such behaviour. The present analysis of sub-categories, because of too small numbers of subjects, is insufficient to provide an empirical answer. Theoretically, of a number of possible generalizations, the following one is preferred. The psychology and pathology of Janet, following the review by Schwartz (20), revolves to a large extent around concepts of drive, tension, aspiration, beliefs and psychological "reserves". Activation and regulation of energy reserves form the basis of the discussion of a variety of disorders. Input and output must be kept in balance to preserve normality, as is neatly expressed in the therapeutic advice given by the following saying:—

*Roste nie—doch haste nie,
Dann hast du nie—Neurasthenie.*

The working hypothesis may be considered that manifest rigidity results from variations in such disturbances of the energy household. If this general hypothesis is pursued, more specific discrimination may be investigated along various lines. Intensity of energy mobilization may represent reactivity to traumatic or other stimuli and may, with advantage, be investigated using theories such as Selye's adaptation level. Adequacy of energy distribution may be thought of as a second aspect of the general problem. This may be investigated using theories of discrimination and generalization. As regards the present experiment, both intensity and adequacy have been represented by respective criteria of intensity of response set (PFCL +2) and adequacy of motivation (many rigidity items). In the latter instance, inadequate achievement motivation, for example, may have resulted in response generalization to unreasonable or unattainable goals.

In the pursuit of such tasks the problem of psychiatric categorization must be considered. Such categories have traditionally been described in terms of *forms* of behaviour (characterology) rather than in terms of variations in *energies* which, consequently, may cause lack of category discrimination by certain aspects of rigidity. The interaction between specific forms of personality and general energy level may result in overtly discriminable behaviour disorders, as described in great detail by Janet.

SUMMARY

Questionnaires of rigidity, extreme response set, drive, neuroticism and extraversion were given to 88 normals and 105 abnormals. Intercorrelations supported the existence of a general factor of rigidity, practically independent of extraversion. Main emphasis was on validation of some specific aspects of the rigidity complex. The rigid personality was shown to be characterized by

extremeness of response, high drive level and abnormality of response. Analyses between normals and abnormals revealed all rigidity measures to differentiate between these groups at a high level of significance. The finding that a scale of "normal" drive was not significantly related to neuroticism, manifest anxiety, or extraversion gave rise to a criticism of some current personality theories of drive. The theories of energy mobilization by Duffy and of energy activation and regulation by Janet are discussed in relation to the above results.

APPENDIX

The appendix contains the item-analysed versions of NR, CPIR, Do, IA and Dr. With the exception of Dr, item number 11 ("Friends have sometimes called me lazy"), all items are keyed for the true response to represent the scale direction. The frequent intermediate response made of "undecided", or "?", is not used. If subjects, against the instruction, decide to use an intermediate response, this is considered in scoring. Two points are scored for an answer in the scale direction and one point for an intermediate response.

The PFCL, added in the appendix, has not been item-analysed properly. It should be considered a preliminary version.

INSTRUCTIONS

Please answer each question by putting a circle round the "True" or the "False" following the question. Work quickly and do not ponder too long about the exact shade of meaning of each question. There are no right or wrong answers, and no trick questions.

REMEMBER TO ANSWER EACH QUESTION

Rigidity (NR)

- | | | |
|---|------|-------|
| 1. You make it a matter of principle never to permit your friends to come between you and your work | True | False |
| 2. Before undertaking a trip, you always plan well in advance and decide on an exact itinerary, from which you are reluctant to deviate .. | True | False |
| 3. The realization of a man's creative work is of greater value than leisure and enjoyment of everyday human relations, which are not important .. | True | False |
| 4. You always prefer the familiar, the safe and sure, to taking chances with the novel and untried | True | False |
| 5. A sound person will always judge another individual's behaviour according to what he would do himself | True | False |
| 6. Whenever the occasion arises to broaden your experience (new job, new residence, travel, etc.), your natural disposition "to belong" makes you reluctant to undertake a change | True | False |
| 7. The following essentials: will-power, determination, perseverance, and independence, are necessary and sufficient to make a true success of one's life | True | False |
| 8. A man ought to concentrate on one task at a time for the sake of doing a thorough job, otherwise he should not undertake it at all .. | True | False |
| 9. There are only a few styles and colours of clothes that you have found to your satisfaction and you would be most reluctant to change to something new | True | False |
| 10. You find it extremely bothersome when unexpected visitors invade your privacy without previous warning | True | False |
| 11. You never compromise on quality but only buy the most solid and lasting things or you do without | True | False |
| 12. Some of your most worthwhile experiences have been (or would be) in associations and talks with persons of great prestige in your field of work | True | False |
| 13. After writing and sending an important letter, you often go over in your mind the possible replies and make alternative plans for action accordingly | True | False |
| 14. Generally you are indifferent to people but you are devoted to a few close to you and dislike intensely certain others | True | False |

Rigidity (CPIR)

- | | | |
|---|------|-------|
| 1. You like to have a place for everything and everything in its place .. | True | False |
| 2. You find that a well-ordered mode of life is congenial to your temperament | True | False |
| 3. You always see to it that your work is carefully planned and organized .. | True | False |
| 4. It bothers you when something unexpected interrupts your daily routine | True | False |
| *5. It is better to be a dead hero than a live coward | True | False |

-6. A strong person will be able to make up his mind even on the most difficult questions	True	False
7. It is hard for you to sympathize with a person who is always doubting and unsure about things	True	False
8. Once you have your mind made up you seldom change it	True	False
9. You have arrived at a conclusive philosophy of life by which you view the scheme of things in their true light	True	False
10. Our thinking would be a lot better off if we would just forget about words like "probably", "approximately" and "perhaps"	True	False
11. For most questions there is just one right answer once a person is able to get all the facts	True	False
12. You set a high standard for yourself and you feel others should do the same	True	False
13. Most of the arguments or quarrels you get into are over matters of principle	True	False
14. Your blood boils whenever a person stubbornly refuses to admit he's wrong	True	False
15. Your hardest battles are with yourself	True	False

Dogmatism (Do)

1. A man who does not believe in some great cause has not really lived	True	False
2. The worst crime a person could commit is to attack publicly the people who believe in the same thing he does'	True	False
3. It is when a person devotes himself to an ideal or cause that he becomes important	True	False
4. Man on his own is a helpless and miserable creature	True	False
5. Unfortunately, a good many people with whom you have discussed important social and moral problems don't really understand what's going on	True	False
6. A person who thinks primarily of his own happiness is beneath contempt	True	False
7. You have often felt that strangers were looking at you critically	True	False
8. It is only natural for a person to have a guilty conscience	True	False
9. To compromise with our political opponents is dangerous because it usually leads to the betrayal of our own side	True	False
10. While you don't like to admit this even to yourself, you sometimes have the ambition to become a great man, like Einstein or Beethoven	True	False
11. To compromise with our political opponents is to be guilty of appeasement	True	False
12. The United States and Russia have just about nothing in common	True	False
13. In a heated discussion you generally become so absorbed in what you are going to say that you forget to listen to what the others are saying	True	False
14. You'd like it if you could find someone who would tell you how to solve your personal problems	True	False
15. On subjects of controversy it is always best to follow the authoritative opinion	True	False
16. I rarely make a decision before asking other people for their advice	True	False

Intolerance of Ambiguity (IA)

1. Today everything is unstable and there is constant change; one never knows what to expect next, which makes one feel uneasy	True	False
2. Certain people are cut out for certain things and are destined for a certain role in life	True	False
3. You always mail your letters immediately upon completion, for it annoys you to leave things in an unsettled state	True	False
4. Talking with a person who speaks indistinctly upsets you	True	False
5. It upsets you not to know exactly what to expect in a pending situation	True	False
6. Anybody worth anything at all does not remain at the bottom of the social scale	True	False
7. It makes you feel uneasy when someone is speaking about something which you do not understand	True	False
8. When you cannot decide what you should do on a personal matter, you always act on the advice of an older person whose judgment you respect	True	False
9. One should avoid doing things in public which appear wrong to others, even though one knows that these things are really all right	True	False
10. It upsets you when you are faced with an ambiguous situation of which you know absolutely nothing of the outcome	True	False
11. One must fight to come out on top in a world made up of the weak and the strong	True	False
12. First impressions about people are usually correct	True	False

13. For most questions there is just one right answer once a person is able to get all the facts	True	False
14. In this world, definite choices must be made all the time	True	False
15. I like to be able to see beforehand how things will turn out	True	False
16. Life is a battle in which the strongest get the prize	True	False
17. One must fight to come out on top in a world which is full of competition	True	False

Drive (Dr)

1. In choosing between two things, it is better to make up one's mind rapidly rather than waste time	True	False
2. I am easily frustrated if I feel that I have not been able to accomplish my best in a task	True	False
3. When doing a task, I feel that my individual reputation is at stake	True	False
4. Frequently I have been the last to give up trying to do a thing	True	False
5. When confronted with difficult tasks I react with great effort knowing I will succeed	True	False
6. If given the opportunity I would conduct a job more efficiently and competently than most people	True	False
7. Whenever I do an important task I find myself extremely involved	True	False
8. I am usually considered a very hard worker	True	False
9. When I set my mind on a task or job I pursue it with relentless determination	True	False
10. In working with others my efforts usually contribute more than those of others	True	False
11. Friends have sometimes called me lazy	True	False
12. I am more motivated than others	True	False
13. If I know I am correct I will go to extremes to prove that my ideas are right	True	False
14. I work much harder than most other people	True	False

Personal Friend Check List (PFCL)

INSTRUCTIONS

Indicate, as shown on the scale below, how you would like your closest friend, of the same sex, to be. There are no right or wrong answers.

For:

—absolutely essential qualities; without this quality the person could not be a friend	score +2
desirable but not essential	„ +1
—no importance is attached to this quality	„ 0
—qualities which are undesirable but which can be tolerated	„ -1
—absolutely intolerable. If a person has this quality he could not be a friend	„ -2

PLEASE RATE EACH WORD

List of words responded to, numbered from 1 to 100 were:

Abstemious, active, adaptable, affectionate, amiable, ambitious, attentive, boastful, broadminded, careless, changeable, charming, cheerful, clean, conceited, confidential, considerate, courageous, cowardly, critical, deceitful, decent, dejected, delicate, dependable, dependent, discreet, dominant, eager, energetic, excitable, faithful, frail, frank, gay, generous, helpless, honest, honourable, humorous, idle, immoderate, immoral, impulsive, indecent, independent, intelligent, intolerant, irritable, jolly, kind, lazy, lustful, lying, malicious, mature, mean, miserable, moral, narrow-minded, obstinate, offensive, patient, pig-headed, popular, proud, quarrelsome, quiet, reliable, reputable, requiring help, restless, rude, sad, selfish, sensitive, sensubus, serious, shy, sickly, sincere, slovenly, stable, strong, successful, sullen, superficial, sympathetic, tactful, tidy, timid, tolerant, uncertain, understanding, unselfish, vain, verbose, vicious, well-known, witty.

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A NOTE ON QUESTIONNAIRE RIGIDITY AND EXTREME RESPONSE SET

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INTRODUCTION

THIS brief report draws attention to some recent results showing that questionnaire measures of rigidity and extreme response set, which are regarded as closely related variables, are likely to possess a much higher degree of generality than usually accepted and that they play an important part in the measurement of normal and abnormal personality.

Reviewers of the literature have frequently expressed "that the status of rigidity as a trait variable is, to say the least, uncertain" (McClelland, 11), or "that the various existing tests of 'rigidity' do in fact measure quite different things and that 'rigidity' as a trait or unidimensional variable is a figment" (Jenkins and Lykken, 10). These statements merely reflect the present research situation but should not be taken to indicate a final verdict on rigidity, as the following recent findings suggest.

In his unpublished thesis, Nigniewitzky (12, 13) demonstrated the existence of a general factor of questionnaire rigidity composed of scales of rigidity, dogmatism, intolerance of ambiguity and fascism. This factor was practically independent of two other dimensions, extraversion and neuroticism.

The Nigniewitzky rigidity scale (NR), which contributed most to the above factor, was subsequently used as criterion in various experiments. The main findings have been that rigidity correlates negatively with motor performance at certain practice stages (2); that, under certain exposure conditions, a negative correlation is obtained between rigidity and a visual immediate recall task (3); that visual learning correlates negatively with rigidity provided sufficient practice is given (7); that, depending on the experimental situation, expressive movement may be enhanced or constricted in the rigid personality (5) and that, specifically under conditions of high ambiguity, verbally expressed confidence in performance correlates significantly with rigidity (4).

These results suggest that adequate measurement of rigidity depends greatly on the knowledge of the exact conditions under which significant interaction between rigidity and performance occurs. In previous research this point has been largely ignored. Instead of using systematic empirical analysis experimental conditions have been determined by theoretical conceptions concerning the mechanism of rigid attitudes.

Much of the future work on rigidity may depend on the development of suitable criteria to be used in the validation of performance variables. The present paper reports briefly on some aspects of the validity of one questionnaire and one adjective check list, employed as criteria in the experiments already quoted. Results are used to guide a more detailed experiment on questionnaire rigidity, which is reported separately (6). Of the two criteria

analysed the NR scale has already been referred to. The second criterion is formed by a measure of extreme response set. This is obtained by means of an adjective check list described in the method section. Of the five response types (+2, +1, 0, -1, -2), the two extreme categories +2 and -2 are analysed, the remaining categories yielding no information important to the present problem. There are indications that extremeness of response is a fairly general characteristic, which is closely related to "intolerance of ambiguity" (14). This in turn is known to form part of the rigidity syndrome. For this reason and for the fact that extremeness of response is implied in most of the rigidity items, extreme response set was expected to represent one form of rigid behaviour. The experiments quoted have in fact confirmed this expectation in that the validity of positive extreme response set has generally paralleled that of rigidity.

METHOD

1. *Questionnaire scores.* The following scores are used:

E=extraversion (24 items)

N=neuroticism (24 items)

NR=Nigniewitzky rigidity (28 items)

PFCL +2=positive extreme response

PFCL -2=negative extreme response } (101 items)

E and N, representing Eysenck's (9) dimensions of extraversion and neuroticism, are used as reference variables. NR is the scale with highest loadings on Nigniewitzky's factor of rigidity (12, 13). The English version of the original French scale, which contained 30 items, has been published elsewhere (4). The extreme response scores +2 and -2 are derived from an item check list modelled on Soueif's (14) Personal Friend Check List (PFCL). The items used are appended. By endorsing 101 items subjects state their opinion as to how much a person must have certain characteristics in order to qualify as a personal friend. Any one of the following five degrees may be used in responding to the individual items: +2, +1, 0, -1, and -2.

In scoring E, N and NR, two points are awarded for a response in the keyed direction and one for responding to a question mark. PFCL +2 and -2 represent the number of respective endorsements to the 101 item check list.

2. *Subjects.* These were collected from the experiments already quoted, with a considerable number added to increase the reliability of results. Computations are based on 146 normals, 108 neurotics and 56 schizophrenics. Separately for sex, subjects distribute as shown in Table I. "Controls I" contains subjects of various occupations not unlike the abnormal groups. "Controls II" is formed by apprentices of a motor car firm. Because of this difference, correlations were first computed separately for these two groups. As, in the process of analysis, no essential differences were noted between Controls I and II they were subsequently combined into one group.

TABLE I
Distribution of Subjects

					Male	Female	Total
Control I	..	..	..	..	35	34	69
Control II	..	..	..	..	77	—	77
Neurotic	..	..	..	..	58	50	108
Schizophrenic	..	..	..	..	26	30	56

Effects due to sex and age have been carefully analysed and were found not to distort the general picture of results. They are not discussed in detail in the present report.

RESULTS

1. *Intercorrelations.* The questionnaire scores were intercorrelated separately for the four sub-groups described in Table I. Results are shown in Table II.

TABLE II
Table of Intercorrelations

			N	NR	PFCL +2	PFCL -2	Age	
E	C I	..	..	-36†	-27*	-02	04	—
	C II	..	..	-12	12	09	15	-15
	Neurotic	..	..	-48†	-20*	10	-12	03
	Schizophrenic	..	..	-02	10	-02	-05	-13
N	C I	..	..	29*	-10	-11	—	—
	C II	..	..	-14	16	-05	0	0
	Neurotic	..	..	31†	02	03	-09	-09
	Schizophrenic	..	..	-12	-03	-04	-29*	-29*
NR	C I	..	..		43†	16	—	—
	C II	..	..		20	19	10	10
	Neurotic	..	..		42†	11	08	08
	Schizophrenic	..	..		30*	08	23	23
PFCL +2	C I	..	..			47†	—	—
	C II	..	..			67†	-05	-05
	Neurotic	..	..			47†	05	05
	Schizophrenic	..	..			39†	09	09
PFCL -2	C I	..	..				—	—
	C II	..	..				09	09
	Neurotic	..	..				-10	-10
	Schizophrenic	..	..				20	20

N: C I=69; C II=77; neurotics=108; schizophrenics=56.

Significance: * = 5 per cent.; † = 1 per cent.

Age: not tested for C I.

The following conclusions may be drawn. E correlates consistently negatively with N, though in the average to a low degree. This agrees with many previous results. All other scores, NR, PFCL +2 and -2, correlate inconsistently and lowly with E and N. The suggestion may be derived that rigidity and extreme response set are largely independent of E and N.

PFCL +2 and -2 intercorrelate consistently to a moderate degree, indicating that extremeness of response is general to positive and negative attitudes. NR, however, is significantly related to PFCL +2 only. To respond in positive extremes is, therefore, a specific attribute of the rigid personality.

2. *Between group differentiation.* Means and standard deviations of all questionnaire scores used are given in Table III. The significance of all group

TABLE III
Means and Standard Deviations of Test Scores

		E	N	NR	PFCL +2	PFCL -2
46 controls	.. $\bar{X}$	23.28	21.56	18.27	9.21	11.67
	SD	9.91	11.61	9.49	7.59	7.51
08 neurotics	.. $\bar{X}$	19.83	33.30	29.51	15.16	19.38
	SD	10.94	11.89	9.31	9.89	9.76
56 schizophrenics	.. $\bar{X}$	20.98	27.66	31.36	20.38	15.04
	SD	9.75	10.22	11.94	15.04	8.89

differences is assessed by t-tests as shown in Table IV. Figure 1 is added to facilitate inspection and demonstrate consistency of results between sexes.

TABLE IV
Significance of Group Differences as Assessed by t-ratios

	E	N	NR	PFCL +2	PFCL -2
Controls vs. neurotics . .	2.62*	7.89†	9.41†	5.43†	7.11†
Controls vs. schizophrenics	1.48	3.45†	8.14†	6.97†	2.71*
Neurotics vs. schizophrenics	0.66	3.02*	1.09	2.67*	2.78*

D.f.: C vs. N=252; C vs. S=200; N vs. S=162.

Significance: * = 1 per cent; † = 0.1 per cent.

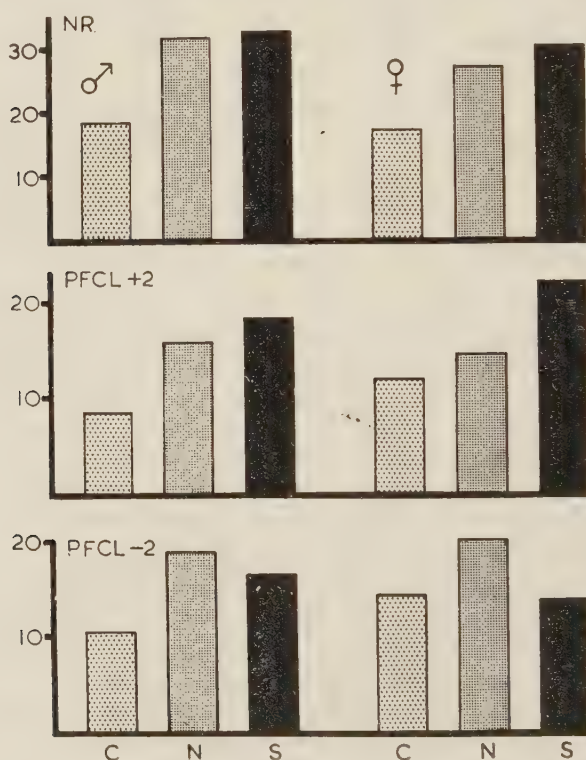


FIG. 1.—Abnormals, neurotics (N) and schizophrenics (S), score significantly higher on rigidity (NR) and extreme positive response set (PFCL+2) than normals (C). On extreme negative response set (PFCL-2) neurotics score higher than schizophrenics.

A number of suggestions may be derived from these data. First it is seen that both abnormal groups score considerably higher on NR, PFCL +2 and -2 than the normals. Rigid behaviour and general response extremeness are therefore typical of the abnormal personality. It is interesting to note that the degree of differentiation between normals and neurotics is as high for NR and PFCL extremes as for N, a scale specifically designed to measure neurotic symptomatology.

Although both abnormal groups respond more in extremes than normals, a specific effect is obtained in that schizophrenics score significantly higher than neurotics on positive extremes while neurotics score significantly higher on

negative extremes. Pending a detailed item analysis this result may be taken to be due to a quite general attitudinal difference between neurotics and schizophrenics, as similar effects have been found in studies using different techniques. Eysenck (8), in an experiment where positively and negatively toned adjectives had to be attributed to photographs of persons, found that neurotics used far more negative adjectives than psychotics. Positive extremeness was furthermore found to be particularly characteristic of the schizophrenic when tested by means of Berg's Perceptual Reaction Test (Barnes, 1).

CONCLUSIONS AND SUMMARY

Questionnaires of extraversion, neuroticism, rigidity and extreme response set were given to 146 normals, 108 neurotics and 56 schizophrenics. It was found that rigidity and extreme positive response set, which intercorrelated significantly, were relatively independent of extraversion and neuroticism. Correlations with various performance scores were quoted to suggest that rigidity of the kind described may play an important part in the measurement of the normal personality.

Particular emphasis was placed on the relevance of rigidity to abnormality. Rigidity and extreme response set differentiated significantly between normals and both abnormal groups. Differentiation was in general as effective as with a neuroticism questionnaire. A specific effect was described showing that schizophrenics score significantly higher on positive extremes than neurotics, while the latter score significantly higher on negative extremes.

APPENDIX

The original PFCL item check list contained the 101 items listed below. A great proportion of these were taken from Soueif (14). A first item analysis, which is not described in detail, showed a number of items to be of little value, predominantly because extreme response frequency was too low. Thus items like "higher economical level", "interested in culture", "politically minded" did not provoke sufficient extreme responses to be useful in the discrimination between individuals or groups. As a result of this analysis, a new scale of 100 items is constructed for further use. This is reported in a separate paper on further validation of rigidity (6).

The 101 original items are now as follows:

Agreeing, always sarcastic, arrogant, attractive as a personality, authoritative/domineering, believing, broadminded, considerate, co-operative, courageous, cowardly, critical of your own attitudes, cultured, dependable, energetic, envious, experienced, faithful, frank, gay, generous, gentle, gloomy, good-looking, good-natured, good reputation, good sense of humour, naughty, helpful, higher economical level than yours, higher intelligence than yours, high moral standards, hypocritical, independent in opinion, industrious, ignorant, interested in culture, interested in religion, interested in social affairs, introverted, keeping his dignity, kind, lacking humour, lacking interest in religious problems, lacking interest in social problems, lacking self-respect, lazy, less intelligent than yourself, lying, miserly, morally degenerate, naive, narrow-minded, neat, obedient, obsessional, obstinate, of bad reputation, of your own political opinion, of your own religion, opportunist, ostentatious, passive, patient, pessimistic, polite, politically minded, poor, progressive, reactionary, rich, rough, same age as you, same economical level as yours, same intelligence as yours, same social level as yours, selfish, sensitive, serious, sincere, social level higher than yours, social level lower than yours, submissive, sulky, talkative, tactful, tactless, tolerant, trustworthy, ugly, unbelieving, understanding, uneducated, unrefined, unselfish, vain, well-balanced, with no respect for others, without sympathy for your own interests, witty, younger than you.

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AN EVALUATION OF IPRONIAZID (MARSILID) IN THE TREATMENT OF DEPRESSION

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IPRONIAZID (1-isonicotinyl, 2-isopropyl hydrazine phosphate) was discovered by Fox and Gibas (1953) whilst working on new synthetic compounds for the treatment of tuberculosis.

Although Iproniazid was found to have therapeutically beneficial effects in tuberculosis it never achieved widespread use and eventually was virtually discontinued because of undesirable side-effects, prominent among which were symptoms due to central nervous stimulation and occasionally psychotic manifestations.

Using a smaller dosage than required for treating tuberculosis Iproniazid has recently been tried in depressed states and enthusiastic reports on its therapeutic effects have been made by Kline *et al.* (1958) and Robie (1958), the latter prophesying that it would supplant electroplexy in all but the most severe depressions.

The central nervous stimulating properties and anti-depressive effects of Iproniazid are thought to be probably related to its biochemical actions as a monoamine oxidase inhibitor (Zeller *et al.*, 1952) and to its effect in causing a rapid rise in the level of brain serotonin (Udenfreund *et al.*, 1957).

Dally (1958) found the drug most useful in mild depressive states rather than endogenous depressions. Verteuil and Lehman (1958) found that about one-third of a group of depressed and apathetic patients showed improvement with Iproniazid. The drug, was however, discontinued because of serious toxic effects which caused the death of a patient from acute toxic liver necrosis.

Further enthusiastic reports on the efficacy of Iproniazid in depression were made at a symposium held in New York in November, 1957 and reported in a special number of the *Journal of Clinical and Experimental Psychopathology* (Supplement to Vol. XIX, No. 2, April, 1958).

These reports, however, do not permit a reliable and valid assessment of the therapeutic efficacy of the drug in depression because adequate controls were not used.

In our opinion, the value as well as the limitations of any new pharmacotherapeutic agent in psychiatric illness can only be assessed by strictly controlled clinical trials.

The fact that many depressive states tend to run a self-limiting course in itself makes controls indispensable. Moreover, many other sources of error need to be taken into account, e.g. the multiplicity of factors relating to the individual or his environment which can influence his clinical state during the therapeutic trial, in addition and independently of the pharmacological effects of the drug.

As the complexity of psychiatric illness makes accurate matching of patients difficult, it is desirable to use the patient as a self control.

The allocation of active drug and the inert preparation used for control purposes should be carried out by a random method to avoid the possibility of bias arising from selection.

The possible therapeutic effects of receiving a course of new treatment either arising from suggestion or from the therapeutic influence of the regime of a new treatment and the associated increased medical and nursing attention.

Further possible sources of error are bias on the part of patient or observer in reporting and recording changes which would tend to occur when it is known when active and inert tablets were being given.

With these considerations in mind a controlled study of Iproniazid in depressive states was carried out using the following methods.

METHODS

1. *Triple-Blind Control*

The pharmacist was the only person who knew when active or inert tablets were being administered. They were identical in shape, size and colour and were given uncrushed to prevent the patient recognizing them by taste.

Each batch of tablets issued by the pharmacist was marked for identification by series of random numbers. Thus physicians, nurses and patients were unaware when active or inert tablets were being administered. The results were fully analysed and assessed before the code was broken, making the method a triple-blind control procedure.

2. *Multiple Recording*

Multiple recording of the patient's clinical state and progress was carried out independently by nurses and physicians.

3. *Special Record Sheets*

Nurses made daily 24-hour recordings of behavioural features. Physicians completed a form, specially designed for the investigation, containing some 18 items (*vide* Table I) relating to behaviour, clinical state and symptomatology. Each item was rated, according to severity, on a 5-point scale (ranging from 0—absent to 4—very marked). The ratings were made by the same physicians throughout the trial at weekly intervals.

4. *Sequence Control*

In view of the possibility that any clinical changes occurring during the trial period might be due to spontaneous improvement or to factors unrelated to the pharmacological actions of the drug, it was deemed essential that the active and inert preparations be given in different sequences in order to ensure that any factor which might influence the patient's clinical state would have the same chance of being coincident with inert tablets as with the active drug.

TABLE I
Mean Ratings of Clinical Features

Clinical Feature	Pre-trial	Iproniazid (I ₁ +I ₂)	Inert Tablets (P ₁ +P ₂)
Depressive appearance	2.9	1.5	1.58
Difficulty in occupying himself ..	1.5	1.4	1.18
Difficulty in making social contact ..	1.4	1.3	1.3
Restlessness	1.4	1.0	0.67
Retardation	1.8	0.4	0.51
Hypochondriacal complaints ..	1.6	0.75	0.51
Depressive speech content	2.0	1.3	1.8
Delusions	0.6	0.34	0.51
Paranoid disposition	0.6	0.33	0.29
Difficulties with eating	1.2	0.95	0.91
Difficulties with sleep	1.7	1.7	1.55
Excitement	0.01	0.01	0
Overactivity	0.12	0.17	0
Hypomania	0	0.01	0
Anxiety	1.9	1.7	1.86
Tension	2.1	1.9	1.95
Perplexity	0.85	0.34	0.48
Aggression	0	0	0.08
Total	16.9	15.4	15.3

I₁=first period of Iproniazid. P₁=first period of inert tablets.
I₂=second period of Iproniazid. P₂=second period of inert tablets.

5. Random Allocation

The allocation of active and inert tablets for the initial three-weekly period of the trial was effected by randomization. Half of the group received Iproniazid during the first three-week period and the other half of the group inert tablets for the same period. Thereafter, three-weekly periods of active drug and three-weekly periods of inert tablets were given alternately for the remainder of the trial. The majority of patients had four periods of three weeks giving a total trial period of twelve weeks. Periods of three weeks were chosen because the findings of a pilot trial showed that when the drug was effective, improvement was usually noticeable in the second week and was usually maximal during the third week.

6. Statistical Methods

The use of parametric tests, e.g. the "t" test, for assessing the significance of differences between two related samples is based on the assumption that the score differences are normally distributed and are measured on an interval scale. As we have no evidence to justify these assumptions for ratings and gradings scores as used in this study, it was considered more appropriate to use non-parametric statistics.

The following non-parametric tests were considered to be specially suitable for the investigations; the Wilcoxon matched pairs signed ranks test (Wilcoxon, 1949; Siegel, 1956) and the Signs test (Siegel, 1956).

7. Criteria for Inclusion in the Double-Blind Trial

All patients taking part in the double-blind trial were in-patients at the Bethlem Royal Hospital. This permitted continuous observation throughout the twenty-four hours and also a strict control over the administration of tablets, which is not usually possible in trials undertaken on out-patients.

After full investigation the patient was discussed at a conference of physicians and staff, and only patients diagnosed as suffering from depressive states were included.

The series consisted of twenty such patients successively admitted, no other criteria being used for inclusion in the trial.

8. *Assessment of Results*

In view of the findings of the pilot study that the maximal effect of Iproniazid usually occurred by the end of three weeks, it was decided to use the assessments and ratings of clinical status made at the end of the third, sixth, ninth and twelfth weeks for comparing the results with Iproniazid with those with inert tablets.

Clinical changes and therapeutic effects were assessed by two main methods. Firstly, the rating scale described above provided a standardized, detailed and quantitative presentation of the patient's clinical state and giving a measure of the patient's overall clinical status by the sum of ratings. It also enables the detection of any differential effects the drug might have on the various aspects of clinical state which is particularly important with Iproniazid which may accentuate some symptoms, e.g. anxiety and paranoid tendencies concurrently with alleviation of depression.

The second method was the grading by the physician of the patient's clinical state based on clinical examination and observation of behaviour and information contained in nurses' reports and record sheets.

A four-point scale with weights was used as follows:

							Weight
Grade I	Not improved or worse	..	..	..	..	..	0
Grade II	Slightly improved	..	..	..	..	..	1
Grade III	Moderately improved	..	..	..	..	..	2
Grade IV	Marked improvement with complete relief of depressive symptoms and signs	..	..	..	..	..	3

By weighting each grade it is possible to make allowance, in a particular patient, for any improvement which occurs with inert tablets, to provide a better measure of the effect attributed to the pharmacological actions of Iproniazid. For example, if a patient showed slight improvement (Grade II = +1) with inert tablets and marked improvement (Grade IV = +3) with Iproniazid, the degree of improvement accorded to Iproniazid would be expressed by the difference in weighting between the respective grades, viz. +2.

RESULTS

RATING SCALES

Table I lists the various clinical features rated on the five-point scale and the mean rating for each for the total group, immediately before the trial, for the two Iproniazid periods combined, and for the two inert tablet periods combined.

When compared with the pre-trial scores, both Iproniazid and inert tablets showed some improvement. But the differences were slight for either individual items considered separately or in total.

The total of all ratings gives a convenient index of the severity of illness and is useful for measuring changes in clinical state during the trial.

Comparison of sum total of ratings before the trial with that of each Iproniazid and each inert tablet period separately revealed the following statistically significant differences.

1. The first Iproniazid period showed significant improvement when compared with pre-trial scores ($P=.015$).

2. The status of the total group at the end of the first three-week period (i.e. I_1 and P_1) showed significant improvement as judged by comparison with pre-trial scores ($P=.048$).

The findings indicated that although Iproniazid had a greater degree of improvement than that associated with inert tablets, the latter (P_1+P_2 combined) also was associated with improvement but the difference did not reach statistical significance ($P=.58$).

The significant degree of improvement in clinical state in the total group at the end of three weeks (i.e. with I_1 together with P_1) indicates that factors other than the pharmacological actions of Iproniazid are operating.

There were no significant differences in the total rating scores between Iproniazid and inert tablets.

COMPARISON OF CLINICAL FEATURES SEPARATELY

If we were to rely on the total ratings alone, detailed changes in the patient's clinical condition might be hidden, particularly any differential effects of the drug on various symptoms. Non-parametric tests have an advantage over the usual parametric tests by enabling comparisons to be made between each item separately. No significant differences were found in any feature between I_1 and P_1 whereas I_2 and P_2 differed significantly in depressive speech content, the difference indicating significantly greater improvement with Iproniazid ($P=.01$).

Both I_1 and I_2 showed significant improvement compared with pre-trial score in depressive speech content ($P=.01$). I_2 also showed significant improvement compared with pre-trial score in restlessness ($P=.05$).

TABLE II
Sum Total of Ratings of Each Patient Before and During Trial

Patients					Pre-trial	I ₁	I ₂	P ₁	P ₂	
1	..	..	..	..	22	15	19	19	22	
2	..	..	..	..	10	9	3	8	15	
3	..	..	..	..	7	5	—	12	—	
4	..	..	..	..	11	10	2	13	7	
5	..	..	..	..	8	9	9	12	13	
6	..	..	..	..	23	13	5	22	5	
7	..	..	..	..	25	25	17	17	17	
8	..	..	..	..	15	14	—	22	—	
9	..	..	..	..	12	12	5	8	14	
10	..	..	..	..	15	7	11	8	8	
11	..	..	..	..	22	18	19	32	12	
12	..	..	..	..	10	12	26	1	10	
13	..	..	..	..	12	13	23	7	14	
14	..	..	..	..	24	13	23	18	13	
15	..	..	..	..	24	11	5	21	8	
16	..	..	..	..	18	14	—	22	13	
17	..	..	..	..	26	7	5	20	19	
18	..	..	..	..	21	16	—	12	10	
19	..	..	..	..	35	24	—	26	—	
20	..	..	..	..	29	37	—	23	—	
Mean of total patient ratings for group					..	18.45	14.7	11.45	16.15	12.5

Thus even with such a detailed method of rating a large number of different clinical features, although revealing some statistically significant differences in favour of Iproniazid, all in all, the beneficial therapeutic effects due to Iproniazid are very modest.

Clinical Gradings

The gradings of clinical improvement associated with Iproniazid and with inert tablets are shown in Table III.

TABLE III

Clinical Gradings at End of 3-Weekly Periods with Iproniazid and Inert Tablets

Clinical Grade	Iproniazid 34 Trials		Inert Tablets 37 Trials	
	N.	Per cent.	N.	Per cent.
1. No improvement or worse ..	15	44.1	13	35.3
2. Slight improvement	12	35.4	18	48.5
3. Moderate	4	11.7	5	13.7
4. Marked	3	8.8	1	2.7
	34	100.0	37	100.0

55.9 per cent. of the group showed improvement with Iproniazid compared with 64.3 per cent. with inert tablets.

If we omit slight degrees of improvement, which are of little importance clinically, and compare moderate and marked degrees of improvement only, Iproniazid has 20.5 per cent. and inert tablets 16.4 per cent. This slight advantage to Iproniazid is not statistically significant.

The device of applying weights to grades permits a more detailed analysis of the results of paired trials with the drug and inert tablets, viz. I_1 compared with P_1 , I_1 compared with P_2 . There were 34 such paired trials of Iproniazid and inert tablets.

The results were:

1. In 13 trials both Iproniazid and inert tablets were identical in grade, viz. 7 showing no improvement or worse (Grade I) and 6 with slight improvement (Grade II).

2. In 11 trials Iproniazid had a higher grade of improvement than the corresponding period with inert tablets. The sum of the weight differences was +11 in favour of Iproniazid.

3. In 10 trials Iproniazid had a lower grade of improvement than the corresponding inert tablet period. The sum of the weight differences was +11 in favour of inert tablets.

This analysis again provides little evidence of efficacy of Iproniazid.

RESULTS OBTAINED FROM AN UNCONTROLLED TRIAL OF IPRONIAZID IN AN ADDITIONAL GROUP OF PATIENTS SUFFERING FROM DEPRESSIVE STATES

Advocates of Iproniazid therapy might claim that two separate three-weekly periods of drug administration was not long enough to produce optimum results and that a longer period with the drug would give much better results.

We therefore present our findings on a larger group of 60 depressed patients who received Iproniazid for periods ranging from 3 weeks to 6 months (Mean = 6 weeks of continuous treatment). This study was not controlled and we wish

to emphasize its limitation on this account for the reasons already given. The results of the double-blind trial provide a salutary check on the findings of this group.

The initial daily dose was 150 mg. in three divided doses. This was gradually reduced when clinical improvement occurred but reinstated if there was a relapse or recurrence of symptoms. The drug was immediately stopped if any toxic effects appeared or if the level of serum transaminase materially increased.

The group consisted of 32 in-patients of the Bethlem Royal Hospital and 28 out-patients attending the Maudsley Hospital.

The diagnostic categories were as follows:

Group 1—Depressive states predominantly endogenous	..	..	19
Group 2—Depressive states predominantly reactive or neurotic	..	..	36
Group 3—Atypical depressive states	..	..	5

The overall clinical state was graded at weekly intervals using the same methods and criteria as in the double-blind study.

The findings are shown in Table V from which it will be seen that only

TABLE IV
Grading of Clinical Status at Completion
of Double-Blind Trial

Classification			1	2	3	4	Other Outcome	Totals
Endogenous	..	..	5	2	0	2	1 mania 1 hypomania	11
Reactive or neurotic	..	..	0	3	1	1		5
Atypical	..	..	1	2	0	1		4
Totals	..	..	6	7	1	4	2	20

TABLE V
Results of Uncontrolled Trial of Iproniazid in 60 Depressed Patients
Clinical Rating

			1	2	3	4	Other Outcome	Totals
Endogenous	..	..	5	5	2	3	1—mania 2—hypomania 1—suicide	19
Reactive or neurotic	..	..	10	12	6	5	2—jaundice 1—hypomania	36
Atypical	..	..	3	2	0	0		5
Totals	..	..	18	19	8	8	7	60

Percentage of total group 30 31.6 13.3 13.3 11.5

16 out of the 60 patients showed either moderate or a marked improvement. Three patients showed a temporary improvement with Iproniazid but relapsed while still receiving the drug. One patient showed a marked improvement regarding retardation but became restless, agitated and later committed suicide.

Even with prolonged administration of Iproniazid, only 26.6 per cent. of the group showed moderate or marked improvement, the results being only

slightly better than those obtained with Iproniazid given for the two three-weekly periods of the double-blind trial. As shown by the latter, part of the improvement associated with the administration of Iproniazid is attributable to factors unconnected with its pharmacological properties.

COMPARISON OF RESULTS OF IPRONIAZID AND ELECTROPLEXY

Eighteen patients who did not benefit from Iproniazid were given electroplexy. Of these sixteen responded immediately making a complete recovery and one showing improvement but not full recovery. Thus only one patient failed to improve with electroplexy. The response to electroplexy was so striking regarding speed and in the degree and quality of recovery, that it left no room for doubt regarding the supremacy of electroplexy over Iproniazid in these patients.

COMPARISON OF RESULTS OBTAINED IN DIFFERENT TYPES OF DEPRESSION

Both in the double-blind trial and in the uncontrolled trial, reactive (neurotic) depressions had somewhat better results than endogenous depressions. The group with the poorest result was atypical depression.

Taking the total 80 patients and comparing moderate and marked degrees of improvement the best results were with reactive depressions (36 per cent.) and the next endogenous depression (23 per cent.) and the worst with atypical depression (11 per cent.).

Special mention must be made of 12 patients of the total of 80 patients studied who showed consistent improvement with Iproniazid and consistently relapsed when the drug was discontinued and subsequently improving when the drug was reinstated. This sequence of events provides additional evidence that the improvement in these patients can be attributed to the pharmacological effects of the drug. These patients comprised 15 per cent. of the total and consisted of 5 with endogenous depressions, 6 with neurotic (reactive) depressions and 1 atypical depression. As a group they showed no particular features or constellations of clinical features in common which would enable them to be selected beforehand.

COMPLICATIONS AND SIDE-EFFECTS

(a) *Physical*

Two patients developed jaundice at a time when their depressive symptoms had considerably improved. A detailed description of these patients is given elsewhere (Benaim and Dixon, 1958).

One patient suffering from hypertension whilst receiving Iproniazid had an episode of cerebral thrombosis which caused a temporary hemiparesis. Iproniazid produced a considerable fall in blood pressure in this patient and the drug was immediately discontinued after the cerebral thrombosis. Such a complication of Iproniazid treatment has recently been reported by Papp and Benaim (1958).

Another patient developed an erythematous rash on the arms and body after drinking alcohol. The rash disappeared when inert tablets were substituted for Iproniazid without the patient's knowledge, but the rash recurred again when Iproniazid was re-instituted when taking alcohol.

One patient had oedema of the legs and a number of patients complained of symptoms due to hypotension, such as palpitations, giddiness and fainting with postural change.

(b) *Psychiatric*

One patient who had suffered from an attack of mania some years previously and who had been severely incapacitated by his present severe attack of depression improved with Iproniazid and was able to start work for the first time in five years, but shortly afterwards became manic even though he was on comparatively small doses of the drug, namely, 25 mg. t.d.s.

Two patients who were relieved of their depression by Iproniazid became hypomanic. Although both had suffered from lifelong mood swings, neither had previously suffered from either hypomania or mania.

Eight patients who were diagnosed as suffering from atypical depressive states derived some relief of depression, this was accompanied by the development of paranoid ideas in six of these, three also showed marked schizophrenic thought disorder. These observations are in keeping with the findings of Hoshimo and Cease (1958) who found no significant beneficial effects with Iproniazid in a group of 64 chronic schizophrenics and of Ferreira, and Freeman (1958) who observed that schizophrenics were sometimes made worse by the drug.

DISCUSSION

During the past year reports on the use of Iproniazid for the treatment of depression have steadily appeared.

The drug was first claimed to provide fountains of energy and to achieve quasi miraculous results in depressive states.

Some early reports claimed striking results. Kline (1958) reported that three-quarters of endogenous depressions responded to Iproniazid as well, if not better than, to electroplexy.

Ayd (1958) later, although using the same dosage in similar patients, had a much lower improvement rate.

In contrast others (Dally, 1958) claim that Iproniazid is most useful for reactive depressions and is not effective in endogenous depressive states.

Such discrepancies between the conclusions made from uncontrolled studies are not surprising in view of the pitfalls already discussed.

Incorrect assessments of the value of a drug such as Iproniazid may arise from clinical heterogeneity of the group; by biased allocation of drug and control tablets; by bias on part of patient or observer in recording clinical changes; by an unequal application of criteria of improvement for active drug and for inert tablets and the manifold unseen factors which may influence the patient's clinical state during the period of the trial.

The present investigation attempted to avoid these pitfalls by using well-defined diagnostic criteria for inclusion of patients for the trial and using a random sample of such patients.

The trial was self-controlled and the allocation of the active and inert tablets for the initial periods was at random followed by alternate periods of active and inert tablets. It was sufficiently long (12 weeks) to allow spontaneous fluctuations in the clinical state to be observed and assessed. The trial was triple blind, the findings were recorded on special forms involving objective as well as subjective data and the results assessed statistically.

The findings clearly show that the improvement occurring with Iproniazid could only in part be due to its pharmacological properties and that other factors contributed, as attested by the improvement associated with inert tablets.

Some clinical features showed a statistically significantly greater improvement with Iproniazid than with inert tablets, in particular, depressive speech content, which is presumably influenced by the euphoriant effect of the drug.

In 15 per cent. of the group there was very strong evidence that relief of depression was due to the pharmacological actions of Iproniazid, as shown by relapse with inert tablets and improvement with the drug, a sequence which was further verified by repetition giving the same results.

The therapeutic effects of Iproniazid appear to be mainly symptomatic, as shown by relapse when the patient is taken off the drug. Prolonged medication was found to result in only a slightly greater incidence of improvement.

The group of patients who benefited most with Iproniazid were not clinically homogeneous, containing both endogenous and reactive depressions.

Our findings with atypical depressions are in keeping with the findings of Hoshima and Cease (1958) and Ferreira and Freeman (1958) that Iproniazid is not helpful in schizophrenics and may cause an exacerbation of the disorder.

Our findings indicate that Iproniazid is less effective than electroplexy for treating endogenous depressions and the results with all types of depressive states are such that it is extremely doubtful whether it is justifiable to continue using Iproniazid in view of its possible dangers and toxic effects.

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SOME RESEARCH INTO THE TREATMENT OF SCHIZOPHRENIA IN THE MENTAL HOSPITAL

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I. INTRODUCTION

BASIC research into the aetiology, physiology and psychopathology of schizophrenia can usually be applied to schizophrenic illnesses wherever they may occur. Each mental hospital however is unique in the area which it serves, the class of patient admitted, and the treatment services and social atmosphere it provides. This means that the results of research projects concerned with the *treatment* for schizophrenia cannot be transferred so readily from one hospital to another. Hospitals treating different groups of patients in a different social atmosphere can produce widely differing results. To some extent therefore each hospital has to determine its own treatment policy, which will be dependent upon its own particular problems and facilities.

Banstead Hospital serves a population of some seven hundred thousand people, the majority coming from South-west London. This area is served by our own out-patient clinics and some patients are referred to the Teaching Hospitals. In general this means that schizophrenic patients who do come to the mental hospital are either those which have failed to respond to treatment elsewhere or those who are severely disturbed in such a way that they cannot be managed at the out-patient clinics, or the Teaching Hospital will not accept them. A considerable number of our patients are socially isolated. They are people who have come either from overseas or from distant parts of England to settle in London but have failed to do so, and now have no friends, work or contacts. At times as many as one in three of the patients on our admission wards for the under sixties are from overseas. This combination of circumstances usually means that the schizophrenic patient has a bad prognosis on the usual criteria, and often means that the prolonged follow-up and supervision which such schizophrenic patients should have will not be available. We are therefore concerned with providing an effective method of treatment for schizophrenic patients which will rapidly relieve acute disturbances, enable a high morale to be developed on treatment wards and which will be effective without long-term supervision. Although our present knowledge suggests that many schizophrenic patients will remain reasonably stable if taking chlorpromazine

indefinitely on an out-patient basis, our problem is that many of our patients will not remain under medical supervision, or will even leave the country.

In a previous paper (Baker, Game and Thorpe, 1958) we reported a comparison of E.C.T., insulin and chlorpromazine therapies as the initial treatment of schizophrenia. Our conclusions were that chlorpromazine given as a two month's course in hospital was the least effective of the three treatments because of a very high relapse rate once treatment ceased on discharge from hospital. We have already pointed out that many of our patients cannot be relied upon for one reason or another to continue taking drugs after discharge. We therefore abandoned chlorpromazine as an initial course of treatment and the project continued as a comparison of E.C.T. and insulin only. At the time of the previous report there were no significant differences in the therapeutic effectiveness of these two treatments.

The present report compares insulin and electroconvulsive therapies used on larger groups of patients than we had obtained previously, and significant differences have now emerged. Further, as it is over three years since the first patients in the scheme were discharged, we are able to give a more meaningful evaluation of relapse rates and some of the more important factors commonly associated with a good or bad prognosis.

II. METHOD

1. *Patients*

All female schizophrenic patients between 18 and 40 years of age, admitted to Banstead Hospital since January, 1956, were included in the scheme if a team of three doctors including two consultants agreed on the diagnosis of schizophrenia, and if the patient had not had previous physical treatment for that condition. As a result of this selection, most of the selected patients either had florid symptoms or a long history of illness. Few had a good prognosis on all three of the common criteria—good previous personality; recent onset and retained affect. They were all treated on the same ward by the same doctors and nurses.

(ii) *Treatments*

Two treatments were compared. The first was a course of 20 electric convulsions given at the rate of three a week (Monday, Wednesday and Friday) for the first twelve treatments, followed by two a week (Monday and Friday) up to the eighteenth treatment, followed by one a week (Wednesday) up to twenty. The treatments were administered with a standard "Ectron" machine and the "Ectonus technique" employed (Russell, Page and Jillett, 1953). Second was a course of 30 insulin comas given at a maximum rate of 1 coma daily for six days a week. All patients received 6 grains of sodium amytal on their treatment days, the E.C.T. group some 60 minutes before the convulsions and the insulin group 45 minutes before the insulin injections. Patients were also given $\frac{1}{160}$ grain of subcutaneous atropine before the convulsion or coma respectively.

(iii) *Allocation of Treatments*

Patients were allocated to one of these two treatment groups by a random selection procedure. In the event of irreversible comas or other untoward effects, where to continue that particular treatment was unwise on clinical grounds, the patient was taken out of the scheme and a more suitable treatment administered.

(iv) *Assessment of Patients*

Patients were assessed immediately preceding treatment on the Wittenborn Rating Scale (Wittenborn and Lesser, 1951), and again one week after completion of treatment. The Wittenborn scale provides ratings for psychiatric symptoms, which are then grouped to give a score on a ten-point scale for the major diagnostic types. Patients were also categorized as Paranoid, Simple, Hebephrenic or Catatonic on the basis of clinical impression and history. A prognostic rating scale was also completed.

(v) *Discharge*

When patients were interviewed one week after completion of treatment, the decision was made whether they could be discharged or whether further treatment or observation was needed. Patients were discharged if they were free from gross symptoms and were able to make reasonable plans for the future. The presence of personality defect, lack of insight, or affective flattening were not, by themselves, considered a bar to discharge. Those patients who were discharged would normally be considered to be recovered or much improved. Patients in whose case the treatment was considered to have failed were next given that treatment considered to be most suitable on ordinary clinical grounds.

(vi) *Follow-up*

Our research psychiatric social worker followed up all our patients after discharge. One of her functions was the accurate recording of relapses, which were defined as occurring if the patient was re-admitted to hospital or sought further medical help for the treatment of her symptoms. Considerable care was taken to follow up our patients, even if they left the country. This involved, for example, a lengthy visit to Ireland where eight patients have lived for some time or other since discharge.

III. RESULTS

Although the two treatment groups were selected on a random basis, it is important to compare their status before treatment on some of the variables which may be associated with a good therapeutic outcome. These comparisons are given in Tables I-IV.

TABLE I
Mean Age and Intelligence Quotient

			Insulin	E.C.T.	Critical Ratio	"p"
Number of patients	..	..	36	37		
Age in years	..	..	33	31	<1.0	NS
Age range*	..	..	18-38	19-39	<1.0	NS
Pre-treatment:						
Mill Hill Quotient	..	..	91.2	79.0	4.2	p<.01
Progressive Matrices Quotient			85.5	76.1	2.1	.05<p<.02
Post-treatment:						
Mill Hill Quotient	..	..	94.3	85.3	3.7	p<.01
Progressive Matrices Quotient			102.1	87.4	2.8	p<.01

* Critical Ratio calculated for difference between standard deviations in age.

TABLE II

Diagnosis

	Insulin	E.C.T.	Chi-square	"p"
Simple schizophrenia ..	7	6	1.73 (3 d.f.)	NS
Hebephrenic schizophrenia ..	3	5		
Catatonic schizophrenia ..	4	6		
Paranoid schizophrenia ..	22	20		
Total	36	37		

TABLE III

Wittenborn Mean Scores before Treatment

	Insulin (36)	E.C.T. (37)	Critical Ratio	"p"
Paranoid schizophrenia ..	6.1	6.9	<1.0	NS
Schizophrenic excitement ..	4.1	4.7		
Hebephrenic schizophrenia ..	2.9	3.8		
Depression	5.1	5.0		
Anxiety	2.5	2.7		

The Wittenborn Scale resolves ratings on 55 psychiatric symptoms into 9 clusters, the scores on each of which can range from 1 to 10.

TABLE IV

Prognostic Factors

	Insulin (36)	E.C.T. (37)	Critical Ratio	"p"
Constitution	.19	.31	<1.0	NS
Duration of illness	.42	.68		
Onset	.48	.69		
Precipitating factor (physical)	.06	.22		
Precipitating factor (emotional)	.74	.62		
Precipitating factor (puerperal)	.29	.28		
Disturbance of affect ..	1.6	1.7		
Incongruity of affect ..	1.7	2.1		
Flattening of affect ..	1.8	1.4		
Body build	2.7	2.2		

FIG. 1.—*Prognostic Items.* (Scores in parentheses.)

Constitution	2 or more close relatives with schizophrenia (2)	1 close relative with schizophrenia (1)	None (0)
Duration of illness	Overt psychotic symptoms appeared more than 2 years ago (2)	Overt symptoms appeared between 1 and 2 years ago (1)	Overt symptoms appeared less than 1 year ago (0)
Type of onset of illness	Insidious—more than 1 year (2)	Insidious but less than 1 year (1)	Acute—less than 1 month (0)
Precipitating factor (physical)	Marked stress (2)	Slight stress (1)	No stress (0)
Precipitating factor (emotional)	Marked stress (2)	Slight stress (1)	No stress (0)
Precipitating factor (puerperal)	Marked stress in puerperium (1)	No marked stress in puerperium (0)	
Disturbance of affect	Severe (3)	Moderate (2)	Slight (1)
Incongruity of affect	Severe (3)	Moderate (2)	Slight (1)
Body Build	Based upon the Rees Index of Body Build for Women (Rees, 1950). Standard scores for each component calculated on the basis of present distributions. Indices above 1.0 were scored 4, between 0 and 1 were scored 3, between 0 and -1 scored 2, and between -1 and -2 were scored 1.		
			None (0)
			None (0)

The Wittenborn Scores in Table III are scaled scores based upon the scoring system developed by Wittenborn and Lesser (1951). Scores in Table IV are mean scores on the variables listed. These variables were scored as indicated in Figure 1.

The immediate results of treatment are given in Tables V-VIII.

TABLE V
Results of Treatment

	Insulin	E.C.T.	Critical Ratio	"p"
Admitted to scheme	36	37		
Completed course	27 (75%)	35 (94.5%)	2.4	.05 > p > .02
Discharged herself against advice ..	2	1		
Medical complications	2	0		
Nursing complications	4	0		
Died	0	1		
Repatriated during treatment ..	1	0		
Completed course and patient discharged	17/27 (62.8%)	29/35 (82.7%)	1.8	NS
Course failed and further treatment necessary	10/27 (37.2%)	6/35 (17.3%)	1.8	NS
Course completed and successful from total patients accepted ..	17/36 (47.2%)	29/37 (78.4%)	2.9	p < .01

TABLE VI
Mean Wittenborn Scores of Patients Who Completed Treatment

	Insulin (27)	E.C.T. (35)	Critical Ratio	"p"
Paranoid schizophrenia ..	2.9	2.4	<1.0	NS
Schizophrenic excitement ..	2.1	2.0		
Hebephrenic schizophrenia ..	1.6	1.9		
Schizophrenic excitement ..	2.1	2.0		
Depression	3.1	2.7		
Anxiety	1.3	1.3		

TABLE VII

Mean Wittenborn Scores of Patients Discharged 1 Week After Treatment

	Insulin (17)	E.C.T. (29)	Critical Ratio	"p"
Paranoid schizophrenia ..	2.0	2.0	<1.0	NS
Schizophrenic excitement ..	1.4	1.7		
Hebephrenic schizophrenia ..	1.2	1.7		
Depression	2.5	2.4		
Anxiety	1.1	1.2		

TABLE VIII

Mean Wittenborn Scores of Patients Requiring Further Treatment

	Insulin (10)	E.C.T. (6)	Critical Ratio	"p"
Paranoid schizophrenia ..	4.4	4.4	<1.0	NS
Schizophrenic excitement ..	3.2	3.8		
Hebephrenic schizophrenia ..	2.4	2.8		
Depression	4.2	4.5		
Anxiety	1.7	1.7		

The patients who were discharged one week following insulin or E.C.T. are compared in Tables VII, IX, X, XI and XII. Table XII was constructed on the basis of the social worker's assessment of the patients' home environments. "Good" means materially and emotionally stable, "Poor" means homeless, and "Medium" means that some home existed.

TABLE IX

Mean Age and Intelligence Quotient of Patients Discharged 1 Week following Treatment

	Insulin (17)	E.C.T. (29)	Critical Ratio	"p"
Age	29	27		
Age range	23-37	19-38	<1.0	NS
Mill Hill Quotient	96.7	85.1	3.2	p < .01
Progressive Matrices Quotient	100.4	87.0	4.1	p < .01

TABLE X

Diagnosis of Patients Discharged 1 Week following Treatment

	Insulin	E.C.T.	Chi-square	"p"
Simple schizophrenia ..	2 (7)	5 (6)	3.5 (3 d.f.)	NS
Hebephrenic schizophrenia ..	1 (3)	3 (5)		
Catatonic schizophrenia ..	2 (4)	5 (6)		
Paranoid schizophrenia ..	12 (22)	16 (20)		
Total	17 (36)	29 (37)		

Figures in parentheses refer to numbers within each category on admission.

TABLE XI

Prognostic Factors for Patients Discharged 1 Week following Treatment

	Insulin	E.C.T.	Critical Ratio	"p"
Constitution	.13	.30	<1.0	NS
Duration of illness	.27	.59		
Onset	.27	.70		
Precipitating factor (physical) ..	.07	.26		
Precipitating factor (emotional) ..	.80	.63		
Precipitating factor (puerperal) ..	.40	.26		
Disturbance of affect	1.54	1.67		
Incongruity of affect	1.54	2.00		
Flattening of affect	1.73	1.40		
Body build	2.20	2.30		

TABLE XII

Assessment of Environment to Which Discharged

	Insulin	E.C.T.	Chi-square	"p"
Good	6	6	2.54	NS
Medium	9	17		
Poor	2	6		

The relapse rates of those patients who were discharged one week following treatment are given in Table XIII, and in Table XIV we have plotted the duration of these patients' remissions up to the present time.

TABLE XIII
Relapse Rates

	Insulin	E.C.T.	Critical Ratio	"p"
Course successful but subsequent relapse to hospital	5/17 (29.4%)	10/29 (34.5%)	<1.0	NS
Course successful but subsequent relapse to O.P.D.	0/17 (0%)	1/29 (3.4%)		
Total relapse following successful treatment	5/17 (29.4%)	11/29 (38%)		

TABLE XIV
Relapse Rates

Date of Discharge							Total Relapse to Hospital
	1-6/56	7-12/56	1-6/57	7-12/57	1-6/58	7-12/58	
E.C.T. ..	100%	50%	40%	25%	25%	14.3%	34.5%
Insulin ..	75%	66%	50%	0%	0%	0%	29.4%
Critical ratio ..	<1.0						<1.0
"p"	NS						NS

In Table XV are given the mean ratings on the prognostic factors given in Figure 1 for the various subgroups of the two treatment groups.

TABLE XV
Relation Between Prognostic Factors and Response to Treatment

			Post-Treatment				After Discharge Follownig Successful Treatment			
			Insulin (27)		E.C.T. (35)		Insulin (17)		E.C.T. (29)	
	Score Expected for Good Prognosis		Success (17)	Fail (10)	Success (29)	Fail (6)	Not Re-lapsed (12)	Re-lapsed (5)	Not Re-lapsed (18)	Re-lapsed (11)
Constitution ..	Low		.13*	.22*	.30*	.50*	.00*	.50*	.18*	.5*
Duration of illness ..	Low		.27*	.67*	.59*	1.00*	.27	.25	.18*	1.3*
Onset ..	Low		.27*	.89*	.70*	.75*	.27	.25	.41*	1.2*
Precipitating factor (physical) ..	High		.07	.11	.26*	.00*	.09*	.00*	.29*	.2*
Precipitating factor (emotional) ..	Low		.80	.77	.63*	.75*	.91	.50	.53*	.8*
Precipitating factor (puerperal) ..	?		.40	.22	.26	.25	.36	.50	.12	.5
Disturbance of affect ..	High		1.54	1.56	1.67	2.00	1.55*	1.5*	1.58	1.8
Incongruity of affect ..	Low		1.54*	1.78*	2.00*	2.25*	1.55	1.5	2.30	1.7
Flattening of affect ..	Low		1.73*	1.78*	1.40*	1.50*	1.73	1.7	1.65	1.0
Body build ..	Low		2.2*	3.5*	2.3	2.0	2.0*	2.6*	2.3	2.3

* Indicates that difference between means is in accordance with expectation (though none is statistically significant). Means not asterisked are not in accordance with expectation.

IV. DISCUSSION

Tables I-IV indicate that the two treatment groups were comparable in age, diagnosis, symptom scores, and prognostic factors immediately preceding treatment. In terms of I.Q., however, the insulin group was appreciably the more intelligent, and the post-treatment quotients confirmed this finding. As the allocation of patients to treatments was done on a strictly random basis, however, this difference in I.Q.s must be attributed to fluctuations in random selection. It is not likely that the slightly superior intellectual level of the insulin group has appreciably affected the results. It is interesting to note in Table I

that the I.Q. increments following treatment are consistent with those previously reported (Thorpe and Baker, 1958), the Progressive Matrices quotients improving by some 10-17 points, and the Mill Hill by some 3-9 points.

Tables V-VII, giving the immediate results of treatment, indicate that there is a statistically significant difference between the percentages of patients completing their course of treatment. Out of 37 patients receiving E.C.T., 94.5 per cent. completed the course. Out of 36 patients receiving insulin, only 75 per cent. were able to complete the course, for the reasons given in Table V. Larger proportions of patients in the insulin group absconded, or had medical or nursing complications during their treatments. The medical complications comprised a severe prolonged coma and a series of epileptic fits during successive comas in spite of anti-convulsant drugs. The nursing complications could conceivably have been prevented if more nurses had been available. Two patients who constantly attempted to abscond while under the influence of insulin had to be taken out of the group, as well as two actively suicidal patients who were considered, after several weeks with no improvement, to be too great a risk. The failures to complete E.C.T. comprised one patient who discharged herself during treatment and another who died. Death was due to renal vein thrombosis in a dehydrated catatonic patient. The suicidal patients in this group soon lost their suicidal tendencies.

The percentages of patients who were considered fit for discharge following treatment were slightly higher in the E.C.T. group, though the difference just failed to reach the 5 per cent. significant level. Similarly, a higher percentage failed insulin therapy though the difference did not reach an acceptable significance level. It should be remembered that the slightly more favourable outcome for the insulin patients may be because only those with a better prognosis completed their course of treatment, whereas almost all the E.C.T. group were able to do so.

Of ten patients who were not well enough to leave hospital following their insulin comas, six had a course of 20 E.C.T.s and were well enough to leave one week afterwards. Three patients had a course of E.C.T., and later of Largactil, without appreciable benefit but all three were eventually discharged while taking Largactil on a maintenance basis. The last patient started a course of E.C.T. but discharged herself prematurely. Of the six patients who were not well enough to leave following their initial course of E.C.T., the two who were considered suitable for comas failed to respond, but both eventually left following rehabilitation and Largactil. The other four all responded to further E.C.T., and Largactil and were all discharged, still taking Largactil on a maintenance basis.

All patients admitted to the scheme, whether they completed their initial course or not, were eventually discharged. All those who showed signs of relapse while in hospital left while still taking Largactil, with the exception of one, who made an excellent recovery following leucotomy. Only one other patient left against advice before completing treatment.

If we regard as a total failure all patients who were either not able to complete their course or who required further treatment at the end of their course, the failure rates for insulin and E.C.T. respectively were 52.7 per cent. and 22.8 per cent. The difference between these percentages is significant at the 1 per cent. level.

The successfully treated E.C.T. patients (i.e. those discharged following treatment) were found not to differ significantly from the insulin successes in symptom scores, age, diagnosis, or in prognostic factors (Tables IX, X and XI)

though they differed significantly in I.Q. in exactly the same way as they had done before treatment was started (Table II). These findings suggest that there were no biases operating in the selection of patients for discharge following treatment in favour of one or other of the two treatments.

The findings also suggest that the two groups of successfully treated patients could be regarded as similar in their ability to maintain their remission after leaving hospital. In this connection an assessment of the home environments to which these patients were discharged was made, and no significant differences between the two groups emerged (Table XII).

The differential relapse rates (Table XIII) showed no significant differences between the two groups, although the relapse rates for E.C.T. were slightly higher throughout, whether "relapse" was taken as meaning relapse to hospital or to out-patient department.

In Table XIV, giving the lengths of time the two groups of patients had to the best of our knowledge maintained their remissions, we see that the percentages of patients relapsing to hospital is a function of the length of time the patients had been out of hospital. Of those patients discharged between January and June, 1956, 100 per cent. of those who had received E.C.T. have relapsed to hospital to date, compared with 75 per cent. of the insulin patients discharged during the same period. For both treatment groups these percentages diminished until we find that of the patients discharged during the last six months of 1958, 14.3 per cent. of the E.C.T. patients have relapsed to hospital to date, compared with 0 per cent. of the insulin patients. It is important to note that there is not a single significant difference in this Table, which serves only to point out that the relapse rates are dependent upon how long ago the patients were discharged rather than upon which of the two treatments the patients received.

An assessment of the value of the prognostic factors has been made in Table XV. It should be noted that in this Table the original groups have been subdivided into smaller groups which has probably contributed to the absence of statistically significant differences. First, to consider response to treatment, the following variables are associated with successful treatment in the direction expected—low constitutional loading, short duration of illness, acute onset, little incongruity of affect, and little affective flattening. It should be pointed out that these factors are associated with successful treatment for *both* treatment groups. The scores associated with maintained remission in the expected direction are a low constitutional loading, and a large physical element as the precipitating factor. These factors also apply to both treatment groups. The failure of the majority of the variables to show the differences which might have been expected between the insulin patients who relapsed and those who did not may be due to the very small numbers of patients in these groups.

The very high relapse rates require further comment. In general it is hospital policy here to consider that patients should return to the community as soon as possible, and we would regard a low relapse rate as evidence of undue caution in our discharge policy. There can be no doubt that regular social worker follow-up leads to a higher relapse rate as we have defined it. This is not only because all relapses are likely to be recorded, but also because a social worker will encourage relatives and patient to seek early treatment rather than await steady deterioration to social isolation. Nevertheless, we suspect that long-term relapse rates in the type of patient we are treating is likely to be very high with or without follow-up. A special report on this problem, comparing the effect of intensive with non-intensive follow-up is in preparation.

Lastly, we should note that the high relapse rate does not mean progress towards chronicity. None of the patients who have relapsed to this hospital have become "long-term" patients here or seem likely to do so. Patients admitted, who have relapsed, are often not so ill as on their previous admission nor so socially disorganized. It is our impression that rapid rehabilitation and an attempt to reintegrate with the community will help the patient to maintain her adjustment, whereas lengthy hospitalization leads to lower morale and greater dependency on others. We also note that our patients usually return to us willingly, knowing that every attempt will be made to help them back into the community. It is essential with this policy to keep in close contact with the relatives and friends where there are any, in order to relieve their anxiety and give them the maximum support. We have found the vast majority of relatives more than willing to help under these circumstances. It seems possible that the combination of physical treatments with active social re-integration is altering the long-term prognosis in this illness.

V. CONCLUSION;

It is apparent from our results that the most satisfactory treatment for this group of schizophrenic patients is E.C.T. It is much more likely that a patient given E.C.T. will complete her treatment and be discharged following it than if she is given insulin comas. This means that ward morale will be high, as the majority of patients will know that following a course of treatment they will very likely be discharged. Both patients and their relatives can make some plans with this expectation in mind. It has become apparent that insulin comas are only likely to be effective in relatively co-operative patients and even then the long-term results are no better than with E.C.T., which is a simpler procedure, causing, in our experience, less distress to the patient. In general, our findings fit in well with our previous report (Baker, Game and Thorpe, 1958) that mental hospitals in the main prefer E.C.T. to insulin for schizophrenia, while teaching hospitals prefer insulin. It is almost certain that this is due to a different type of patient being treated in a different social situation.

We would like to make it clear that physical treatments are not regarded as the only factor in recovery for our patients. At present however we know of no way of managing the type of patient we are admitting without their use. We think that both E.C.T. and insulin comas lead to a temporary disruption of the patient's relationship with the world around her, and that when she recovers from this she is able to form better human relationships in the calm emotional atmosphere of our treatment wards.

Lastly, it would seem that the prognosis for schizophrenic illnesses is being altered by modern methods of treatment and insistence on re-socialization. We are not seeing the steady deterioration which was reported in up to one-third of schizophrenic admissions in the past. On the other hand we are having a very high relapse rate for reasons which have been discussed. This study has only been running for three years and a further period of follow-up may alter our conclusions once again. It is clear that research in the mental hospital must be continuous and full recognition be given to social trends as well as immediate treatment policies.

VI. SUMMARY

Some research on the treatment of schizophrenia in a mental hospital is described.

Two groups of schizophrenic patients were formed on a random selection

basis, and were treated with 30 insulin comas and 20 E.C.T.s respectively. The results of these treatments showed that a higher proportion of insulin patients were unable to complete their course of treatment. Of these patients completing treatment the difference between the percentages of patients discharged was not statistically significant.

Assessments of a variety of prognostic factors were made and many of them proved to be consistent with expectation, though not statistically significant.

Research should be attempted which will show the influence not only of current therapeutic techniques, but also of social attitudes.

VII. ACKNOWLEDGMENTS

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A CONTROLLED STUDY OF POST-PARTUM MENTAL ILLNESS

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ALTHOUGH modern opinion recognizes that there is no such entity as puerperal insanity, views on the part played by the pregnancy in producing mental illness are not so unanimous. The fact that the onset of a patient's illness is related to the puerperium is considered by some authors to have a favourable, and others an unfavourable, prognostic significance. Puerperal mental illness achieves the distinction of separate identification in the International Nomenclature of Disease, not as "Schizophrenia in association with the puerperium" or "Manic depressive psychosis in association with the puerperium" but as Puerperal Psychosis, 688.1.

The relationship between mental illness and the puerperium may be one of three possibilities. Firstly, there may be no relationship at all, when one would expect the pattern of the illness and its outcome to be similar to that of a patient who had not been pregnant. Conversely the effects of the puerperium may be causal, when one would expect a unique pattern of illness, each case similar to the others and differing from other forms unrelated to pregnancy; such an illness would never occur for example in males, or after the reproductive period was passed.

The third possibility is that the puerperium acts as a stress situation which precipitates the illness in a predisposed personality. If it were correct that it is acting as a simple stress, then other stresses would be expected to produce a similar type of illness which would have the same natural history and response to treatment. The stress of the puerperium may however be unique, not reproducible by economic, domestic or social stresses, those that are more obviously seen affecting non-puerperal patients. It is well recognized for example that vigorous hormonal changes are taking place as pregnancy is replaced by lactation. In that case, although the general pattern of the various illnesses would be similar to that of non-puerperal mental illness, one would expect there to be differences both in symptomatology and outcome.

A study of the extensive literature on the subject of mental illness in association with pregnancy and the puerperium reveals a remarkable lack of consistent conclusions concerning aetiology; similarly there is no uniform opinion on prognosis. Yet it is of great importance to be able to offer to the patient and her husband information concerning the duration and outcome of her illness as well as the probability of recurrence in association with, or independent of, future pregnancies. For this reason I have studied a series of patients who have been in my care, some of them under the supervision of a senior colleague, during the past 5½ years. All of them were admitted with a mental illness starting from within a few days to two months after a confinement. Mental illness commencing during the gestational period has not been included.

Tetlow (1955) has shown that the great majority of cases of mental illness associated with childbirth occur in the first month after confinement.

This group has been followed up and compared with a group of women, also in my care, who were in hospital at approximately the same time and matched for age and diagnosis with the puerperal group. There has also been opportunity to study a group of normal women in an obstetric unit who have recently been delivered.

REVIEW OF THE LITERATURE

Puerperal insanity has been described for many centuries. Zilboorg (1928) quotes a description by Hippocrates, and Boyd (1942) refers to Celsus, Galen and Soranus who recorded instances of post-partum psychoses. Boyd also points out that Marcé in 1858 concluded that there was no form of insanity which could not occur in relation to the puerperium. Yet the literature of the second half of the 19th century has many reports of insanity of pregnancy, the puerperium and lactation, this nomenclature being considered aetiologically descriptive.

Accepting that there is no specific entity of puerperal psychosis, the part played by the puerperium in the production of mental illness, if it plays any part at all, must be that of precipitating factor causing one of several types of illness with the same general pattern as those of non-puerperal patients. Why then do some patients develop the illness and others escape? Presumably because of predisposition on the part of the patient allowing the causative effects of the puerperium to act.

Considering these causative effects, the likely possibilities are physical and endocrine, and economic, social and individual psychological stresses. The physical causes are those which are likely to produce the toxic-confusional or delirious picture, and it is noticeable that with the extensive use of antibiotics this type of reaction is increasingly uncommon. Clarke (1913) considered toxic factors were not important, but Strecker and Ebaugh (1926) report 34 per cent. due to toxic factors, Solomons (1931) considered toxæmia, sepsis and chorea the most usual factors, and Parfitt (1934) found eight cases with subinvolution and four with pyrexia out of fourteen cases. James (1935) grouped psychoneurotic reactions with toxic deliria and these together formed a third of all cases. Harris (1936) reporting 45 cases admitted from 1931 to 1934 had eight patients with a delirious type of illness. Only one of these had an obvious toxic focus, a carbuncle. Piker (1938) reviewing the literature concerning cases associated with childbirth found 35 per cent. of psychoses of 891 cases due to toxic exhaustion. Cruikshank (1940) had an incidence of 38 per cent., Boyd (1942) 28.5 per cent. with some cases proceeding to more clear-cut manic-depressive or schizophrenic illness. Smalldon (1940) found only 3.6 per cent. of his cases were of toxic-exhaustive type, but adds that such factors were frequently noted as precipitants of depressive illness. Jacobs (1943) found 50 per cent. and Skottowe (1942) mentioned physical complications in more than half of his cases.

Then suddenly the pattern changes: Brew and Seidenberg (1950) describe 7 per cent., Hemphill (1952) in a review of the ten years 1938-48 found 20 per cent. but in a second series since 1948 found no cases. Tetlow (1955) found no difference in the incidence of obstetrical complications between a group of patients suffering from psychosis of childbearing and normal puerperals, the incidence of infection being 7.5 per cent., Vislie (1956) described 4.5 per cent.

of his cases with severe puerperal infection producing symptomatic psychosis and White *et al.* (1957) found no cases of toxic confusional psychosis. Madden *et al.* (1958) do not mention this diagnosis in their categories. Martin (1958) found 2.6 per cent. in her 75 cases. While some of the papers are describing gestational as well as puerperal mental illness, the incidence of delirious reactions is low in the former type of patient. It is apparent that there is a sharp fall in the incidence of this form of illness. The incidence of puerperal illness is always difficult to assess but Herzer (1906) gave 2.5 per 1,000, Hemphill (1952) 1.4 per 1,000, Tetlow (1955) 1.5 per 1,000 and it is possible that this fall is due to the reduction in the number of cases due to toxic conditions.

There still remain, however, many cases of puerperal mental illness and other factors must therefore be responsible. It has always been considered likely that considerable endocrine disturbance must take place at the puerperium; it has been suggested that this is in fact the cause of onset of labour, the diminishing sedative effect of the corpus luteum hormone leaving the unrestricted action of pituitary and follicular hormones on the gravid uterus (Strachan, 1947). However, Karnosh and Hope (1937) found that values of prolactin and oestrin estimations did not differ appreciably from those from non-puerperal women. Hemphill (1952) mentions that the lack of response to E.C.T. and insulin points to a serious endocrine imbalance, since such treatments operate through their effect on endocrine equilibrium; other workers, however, do not agree that such a poor response to treatment is usual. Wilson and Christie (1925) used ovarian extract, the value of which was considered to be due to its effect of re-establishing menstruation. Davidson (1936) also treated patients with ovarian and thyroid hormones.

Bayliss (1955) describes the variations in plasma steroid level during pregnancy and the puerperium noting that the mean level returned to normal by the eighth post-partum day, but there was marked individual variation. He concludes that the main sources of the increase lie in the maternal adrenals and to a lesser extent in the placenta. Bower and Altschule (1956) treated relapsing cases of post-partum psychotic depression with progesterone because they considered the relapse to be due to hyperfunction of the adrenal cortex. Delay *et al.* (1948) considered the primary disorder to be found in the hypophyso-diencephalic regions, producing both puerperal psychosis and histological changes in the endometrium. Laboucarié (1949) did not confirm this hypothesis.

General economic, social and religious factors have been considered of importance. Karnosh and Hope (1937) found an increased incidence of puerperal psychosis during the American depression but Brew and Seidenberg (1950) found a drop during the war years and Hemphill (1952) noticed no important influence on the number of admissions with puerperal illness during the same period, though no details are mentioned. Vislie (1956) on the other hand found an increase in Norway during the war years, particularly of the neurotic type of illness. Strecker and Ebaugh (1926) and Smalldon (1940) mention a high incidence among Jews, but this is not confirmed by Brew and Seidenberg (1950) nor Fondeur *et al.* (1957). If social pressures are important one would expect a high rate after illegitimate conceptions and births. Tetlow (1955) found a high proportion of single women (10 per cent.) in his series and a further five had children as a result of an extra-marital conception and three pregnancies were the result of an incestuous union, while only one normal control and one non-puerperal psychotic woman had an illegitimate pregnancy. However, he had the impression that this situation was not as disturbing to the patient as one might have expected. Kasanin (1940) reports a similar experience. One must

expect such factors to play an important part in the illness though they may be responsible for the form of the illness and the thought content rather than for the production of the illness. Jacobs (1943) noted the importance of psychological conflict as a precipitating factor and suggested psychotherapy during pregnancy in appropriate cases. Skottowe (1942) commented on the frequency of mental strain present in 80 per cent. of his cases.

White *et al.* (1957) also emphasize the effect of such factors as unstable marriage relationships and financial strain as a result of the pregnancy, in the production of the illness. Fear of pregnancy, erroneous ideas due to inadequate knowledge, "old wives' tales", memories of previous illness, can also play their part in affecting even a normal pregnancy (Tylden, 1950).

The predisposition of the patient has also to be considered and two factors are of importance, heredity and the premorbid personality of the woman.

The assessment of hereditary factors is not usually easy since patients may not know or be unwilling to divulge information and even where facts are known, only criteria such as admission to hospital or suicide are likely to approach reliability and even these factors must depend on the prevailing culture pattern. This uncertainty is reflected in the wide range of incidence of hereditary factors found by different workers; Cruikshank (1940) found 32 per cent., Skottowe (1942) 50 per cent., Hemphill (1952) 14·5 per cent., Vislie (1956) 75 per cent., Tetlow (1955) 25 per cent.—this being significantly greater than in his group of non-puerperal women with psychosis, and Martin (1958) 32 per cent.

Several workers have commented on the premorbid personality of the patient who develops post-partum mental illness. Opinions are conflicting, since some workers believe that previous personality is significant while others take the opposite view. Zilboorg (1928) suggests that schizophrenia develops only in a sexually frigid, aloof schizoid personality. Cruikshank (1940) found a high incidence of pre-psychotic instability and Boyd (1942) mentions immaturity, and anxiety concerning the event. Hemphill (1952) describes a dependent, over-anxious, obsessional, rigid personality which results in an entity, puerperal depression which differs in outcome from non-puerperal depression. Tetlow (1955) found evidence of a personality predisposition with sexual and reproductive inadequacy though evidence for this is not fully presented.

White *et al.* (1957) found evidence of long standing maladjustment and immaturity, although in another paper by the same workers (Fondeur *et al.*, 1957) the comment is made that there is no unusual premorbid personality.

Anderson (1933) in a controlled study found no material difference in the pre-psychotic sexual life of groups of puerperal and non-puerperal psychotic women. Martin (1958) could draw no definite conclusions from her series but found that fourteen of her fifteen schizophrenic patients showed no clear pre-psychotic schizoid features.

The form of the illness and its outcome have also received much attention and again there is conflicting evidence. Comment has already been made on the fall in incidence of delirious reactions, and in more recent papers the main groups described are manic-depressive psychosis, schizophrenia and neurotic reactions. While the incidence of delirious reactions has fallen, mention of neurotic illness has become rather more common. Strecker and Ebaugh (1926) found 2 per cent. in their series, Parfitt (1934) no cases, Boyd (1942) 6 per cent. and Hemphill (1952) 6 per cent. (this is a series spread over 14 years). The fact that there is an increase in the number of patients on whom this diagnosis is made does not necessarily indicate an increase in incidence of neurotic reactions. It is likely that

with a greater awareness of the possibility of neurotic illness and an increase in the number of non-statutory beds, more patients are coming to the attention of the psychiatrist.

While the usual reference to the form of the illness is that it follows, in general terms the pattern of the non-puerperal illness, Armstrong-Jones (1923), McIlroy (1928), and Smalldon (1940), mention the high incidence of infanticidal impulses and Frumkes (1934) found a frequent delusion that the child was dead. Brew and Seidenberg (1950) describe actual or symbolic rejection of the child as a universal finding. Tetlow (1955) also found evidence of an abnormal emotional relationship with the child in cases of affective psychosis but less marked in schizophrenia.

Hemphill (1952) has described puerperal depression differing from manic-depressive psychosis and in many ways resembling involutional melancholia. The personality is rigid and restrictive, the illness presents with agitation, depression, ideas of guilt and unworthiness and the condition is extremely intractable though eventual recovery is usual. Hegarty (1955) describes post-puerperal recurrent depression, a relapsing depression related to the premenstrual period and consequent on mild puerperal depression.

Hemphill (1952) also comments on the poor prognosis for schizophrenia as do Skottowe (1942), James (1935), and Boyd (1942). Brew and Seidenberg (1950) find the prognosis poorer than in affective states, while Armstrong-Jones (1923), Parfitt (1943), Harris (1936), Smalldon (1940) and Wick (1941) described a good eventual prognosis prior to the advent of modern physical treatments. More recently Polonio and Figueiredo (1955), Vislie (1956), Fondeur *et al.* (1957), and Martin (1958) also found the outcome in schizophrenia satisfactory.

The prognosis of puerperal mental illness can only be satisfactorily examined in relationship to that of a similar group of women suffering from non-puerperal mental illness of the same type. Controlled studies are essential if one is to assess the effect of the puerperal aspect of the illness. The number of studies with a comparable group of non-puerperal women with mental illness is small, and those that are found do not always have a follow-up of the patients. Tetlow (1955) compares a group of puerperal and non-puerperal women both suffering from mental illness and also describes puerperal patients without mental illness. He describes general aetiological factors but does not give clinical details of the psychiatric illness. There is no follow-up. Polonio and Figueiredo (1955) review the clinical records of a group of puerperal mental patients and compare them with a non-puerperal group. White *et al.* (1957) compare 100 cases of post-partum mental illness with a similar group matched for age and year of admission and also describe follow-up studies. Seventy-five per cent. were reasonably well after four years, while one in seven may be expected to have a further illness in association with a subsequent pregnancy.

Consideration of the extensive literature on the subject shows a number of faults. It is common for cases of mental illness occurring during pregnancy and after to be grouped together, yet it seems likely, both from a psychological point of view, and also that of hormone balance that these periods may be dissimilar. Even more apparent is the lack of control studies, and yet conclusions are drawn concerning prognosis without reference to patients who have not been pregnant. The retrospective study of case notes suffers from the disadvantage that data are not always accurately recorded, while patients looked after by different physicians cannot necessarily be expected to achieve the same response to treatment. Follow-up studies are also necessary before the question of whether further pregnancy is advisable can be satisfactorily answered.

The present paper describes an attempt to remedy some of the defects which have been mentioned.

METHOD

When carrying out a scientific study it is important to maintain constant all variables except the one under observation. In clinical research this is manifestly impossible, since many factors are outside the control of the investigator. One method of circumventing this problem is the use of large series in the hope that minor variations will cancel each other out. An alternative is a detailed study of a small group with efforts made to study the factors responsible in order to minimize or remove their effect on the investigation. This includes both medical and environmental factors, since in addition to the purely physical methods of treatment given to the patient many factors, broadly grouped together as the therapeutic environment, play their part in the eventual outcome of a patient's illness. Even the effect of drugs may vary, depending on both internal and external environmental factors (Marley, 1959). The type of ward and hospital, the attitude of staff and patients, the relatives and neighbours, all produce their own effect contributing to or diminishing the therapeutic effort.

In an attempt to reduce at least some of the variables in this study, I have limited investigation to patients with post-partum mental illness treated by myself, though at times under the supervision of a senior colleague and have paired with them non-puerperal patients who were in hospital during approximately the same period. In this way my own knowledge and experience has been constant for each pair and so, to some extent, has the ward environment. Patients were paired for age and also for diagnosis utilizing the final diagnosis arrived at on discharge from hospital. There was no attempt at pairing details of clinical state or background.

The cases were two series, each of 42 patients, admitted to hospital during the period July, 1953 to March, 1959. One group were suffering from a mental illness occurring in close relationship to the puerperium—i.e. within two months of the date of delivery. Patients whose florid illness commenced during pregnancy were not included, though some patients, on questioning, described retrospectively minor prodromal symptoms. The second group were diagnosed as having similar mental illnesses but not related to the puerperium.

I also had the opportunity of examining a group of 42 patients in the Department of Obstetrics. These patients, unselected, had been recently delivered, and were not considered to be suffering from overt mental illness.

The diagnosis of patients with mental illness was made on the clinical history and psychiatric state together with additional information from relatives.

It is self-evident that the diagnosis of endogenous depression could not be restricted to cases without evidence of reactive factors, since in all cases there was the puerperium which could be considered a reactive factor. Diagnosis was based on the following criteria, several of these features being present to substantiate a given diagnosis:

1. *Endogenous depression.* Deep depressive affect with delusions of guilt, unworthiness or hopelessness. Suicidal thoughts or attempt. Restlessness and agitation or retardation. Slowing of thought processes. Early waking type of insomnia. Lack of insight.

2. *Neurotic depression*. Labile depression, clearing temporarily when in cheerful surroundings or company. Anxiety symptoms both somatic and mental. Phobias. Lack of delusional ideas. Difficulty in getting to sleep, unpleasant dreams.

3. *Anxiety state*. Somatic symptoms—palpitation, headaches, dyspepsia. Phobias, panic states. Affect predominantly of fear.

4. *Schizophrenia*. Bizarre manneristic behaviour. Bewilderment and perplexity. Involved or circumstantial speech. Blocking of speech. Incongruous or blunted affect. Bizarre hypochondriacal or paranoid delusions, auditory hallucinations. Lack of insight. Clear sensorium.

Manic states were not found nor were toxic-confusional states. However, the diagnosis between toxic-confusional states and schizophrenia or endogenous depression was not always easy; in the early stage retardation or perplexity may give the appearance of confusion and disorientation. Further observation clarified the picture.

Although some authorities, Feldman *et al.* (1946) and Impastato and Gabriel (1957) suggest there is a danger of embolism if electroplexy is given too soon after delivery, this was not considered to be a contra-indication to treatment where it was indicated and each patient received electroplexy, insulin coma, tranquillizing drugs or psychotherapy separately or together, according to psychiatric indications based on the diagnosis.

All but three recent admissions in each of the groups with mental illness were discharged from hospital after the illness under observation, though some of each group have subsequently been re-admitted. Both groups of patients have recently been visited by a social worker to assess their present status. The follow-up period varies from six months to five years since discharge from hospital. The social worker noted the present behaviour of the patient, together with confirmatory evidence from a relative where possible, the attitude of the patient to the child born prior to the illness and whether there had been further pregnancy or further mental illness, and any temporal association between them.

The non-psychiatric patients in the obstetric wards have not been followed up, but since there is only one mental hospital serving the area, it is unlikely that a patient would be admitted elsewhere, and none of these patients had been admitted up to a month after confinement.

The three groups of patients were studied from the following points of view where applicable:

1. Previous history, family history and premorbid personality.
2. Obstetric history, particularly in relationship to the immediate pregnancy.
3. Other stresses occurring immediately prior to the onset of the illness.
4. Symptomatology and response to treatment.
5. Follow-up results of the patients with mental illness. Attitude of patient towards further pregnancy, towards the husband, and the child which was born at the time of the mental illness.

RESULTS

Each group consists of 42 female patients and will be referred to as the puerperal mental illness group, the non-puerperal mental illness group and the normal puerperal group respectively and results will be given in this order.

The age range is 19 to 42 years, average 30.0 years in the puerperal mental illness group, 19 to 42 years, average 30.0 years in the non-puerperal mental illness group and 21 to 43 years, average 31.6 years in the normal puerperal group.

The number of patients who had undergone one or more pregnancies are shown in Table I.

TABLE I
Number of Pregnancies Undergone by Patients in Each Group

	Nil	Primi- para	Multiparous			5 or More
			2	3	4	
Puerperal mental illness ..	—	16	11	10	3	2
Non-puerperal mental illness ..	21	10	6	4	1	0
Normal puerperal ..	—	12	12	7	1	10

A chi-squared test shows there is no significant difference between the numbers of primiparous and multiparous patients in the two puerperal groups ($\chi^2=1.07$; $p>0.1$). Because several of the non-puerperal group were unmarried and others childless, the relationship of numbers of children cannot usefully be compared with the other two groups.

Other personal data which were considered relevant were the numbers of patients who had had previous mental illness, this being recognized by admission to a mental hospital, and a family history of mental illness, using a similar criterion.

TABLE II
Incidence of Previous Mental Illness in Patient, Parents and Siblings

	Previous Psychiatric Illness		Family History of Psychiatric Illness		
	With Preg- nancy	Without Preg- nancy	Paternal	Maternal	Sibling
Puerperal mental illness ..	6	6	2	9*	0
Non-puerperal mental illness ..	3	3	4	8†	1
Normal puerperal ..	1	2	1	6	0

* Two patients' mothers had puerperal psychosis, one after the patient's birth.

† One patient's mother had puerperal psychosis.

In assessing premorbid personality, five categories were used, relying on the patient's own description and supplemented in the case of the mentally ill patients by information from relatives. The groups were:

- (a) Schizoid—shy, reserved, isolated with few outside interests.
- (b) Anxiety-prone—a worrier, with minor preoccupations, afraid of meeting people.
- (c) Obsessional—meticulous, houseproud, conscientious.
- (d) Extraverted—good company, mood swings, many friends, outside interests.
- (e) Other—usually placid, with no marked tendencies in the direction of one of the other four types.

The incidence of the different types of personality is shown in Table III.

TABLE III
Premorbid Personality of Three Groups of Patients

	Schizoid	Anxiety Prone	Obsessional	Extroverted	Other
Puerperal mental illness ..	7	25	1	2	7
Non-puerperal mental illness ..	12	19	4	2	5
Normal puerperal ..	0	17	0	2	23

A chi-squared examination was carried out to examine the relationship between the premorbid personalities considered predisposing to mental illness, that is—schizoid, anxiety prone, obsessional and extraverted, in those suffering from mental illness as compared with the normal puerperal group. Summing the number of patients with predisposing personalities with mental illness and comparing them with the normal puerperal patients, there is a highly significant difference between the two groups ($\chi^2=22.9$; $p<0.001$). It is unnecessary to carry out statistical examination of the results of the two mentally ill groups, since inspection of the table shows that with thirty-five of the puerperal mentally ill and thirty-seven of the non-puerperal mentally ill having a personality predisposing to mental illness and seven of the former and five of the latter having a placid personality, there is manifestly no difference between these two groups.

The next point to be considered is the situation before and during the pregnancy to assess the effect of such factors as personal stresses and obstetrical complications. In the non-puerperal group the incidence of personal stresses was also noted. The type of stresses found were domestic, where the breadwinner was ill or deceased, marital strife or personal illness such as influenza. The incidence of premarital conception, illegitimate births (nil found) was noted and the mother was questioned concerning her attitude towards the pregnancy as to whether there was positive desire for a child, accidental but not unwanted conception, or a definite annoyance or anger at the prospect of a child. Obstetrical complications such as breech presentation, Caesarean section, or Rh. factor incompatibility were noted.

TABLE IV
Incidence of Reactive Factors

	Personal Reactive Factors	Premarital Conception	Unwanted Pregnancy	Obstetrical Complications
Puerperal mental illness ..	7	2	5	13
Non-puerperal mental illness ..	16	Not applicable		
Normal puerperal ..	7	0	4	24

The diagnostic categories of the two groups of patients with mental illness have already been defined. In none of the patients seen in the Obstetrical Wards was there evidence of severe mental illness although some patients showed definite anxiety symptoms. None of these patients has since been admitted to the mental hospital, though the patients have not been followed up at home.

The number of patients in each diagnostic category is summarized in Table V; since the groups were paired for diagnosis the numbers are the same.

TABLE V
Number of Patients in Each Diagnostic Group

Schizophrenia	..	..	..	..	..	..	..	..	15
Endogenous depression	..	..	..	..	..	..	..	..	10
Neurotic depression	..	..	..	..	..	..	..	..	12
Anxiety state	..	..	..	..	..	..	..	..	5

The time relationship between the date of parturition and the onset of symptoms was noted and also the delay between onset of symptoms and admission to hospital. Similarly the duration of symptoms prior to admission to hospital in the non-puerperal group was noted. The results are summarized in Tables VI and VII.

TABLE VI
Onset of Symptoms After Parturition

		Schizophrenia	Endogenous Depression	Neurotic Depression	Anxiety State
First week		5	4	5	1
Second week		2	2	3	2
Fourth week		2	0	2	0
More than six weeks		5	3	1	2
Not known		1	1	1	0

TABLE VII
Time of Admission to Hospital After Onset of Symptoms

	Schizophrenia		Endogenous Depression		Neurotic Depression		Anxiety State	
	Puer-peral	Non-Puer-peral	Puer-peral	Non-Puer-peral	Puer-peral	Non-Puer-peral	Puer-peral	Non-Puer-peral
Less than								
1 month	.. 5	3	3	0	4	0	1	0
1-2 months	.. 6	4	2	0	0	2	2	2
2-6 months	.. 4	6	4	2	4	3	1	1
More than								
6 months	.. 0	2	1	8	4	7	1	2

The majority of patients develop symptoms within one month of confinement, but Table VII shows that this does not mean they are necessarily admitted to hospital at that time. However, the patients with puerperal illness tend to seek admission, or possibly to be admitted, earlier, presumably because the inability to manage the extra work involved with a new baby draws attention to the mental illness. Comparing the patients admitted within eight weeks of onset of symptoms with those admitted after symptoms have been present for eight weeks, there is a significant difference between the puerperal and the non-puerperal group ($\chi^2=7.1$; $p<0.01$).

After treatment, the patient was able to be discharged in the majority of cases, with only three recent admissions still in hospital. Some patients took their own discharge. As will be demonstrated in the follow-up study, a number of patients were re-admitted. The condition of the patient at the time of discharge was classified as "Recovered" if she was symptom-free and able to return to her normal work. If there were marked symptoms which prevented full return to activity she was classified "Relieved" and "Not Improved" where there was persistence of the original symptoms to a severe degree.

Table VIII gives the number of patients in each group.

TABLE VIII
State of Patients on Discharge

		Schizophrenia—15 Pairs			
		Recovered	Relieved	Not Improved	In Hospital
Puerperal mental illness	..	6	4	2	3
Non-puerperal mental illness	..	9	6	0	0
		Endogenous Depression—10 Pairs			
Puerperal mental illness	..	5	5	0	0
Non-puerperal mental illness	..	7	3	0	0
		Neurotic Depression—12 Pairs			
Puerperal mental illness	..	6	4	2	0
Non-puerperal mental illness	..	4	8	0	0
		Anxiety State—5 Pairs			
Puerperal mental illness	..	4	1	0	0
Non-puerperal mental illness	..	4	1	0	0

No attempt is made to describe individual treatment but in general patients with psychotic illness received physical treatments—electroplexy, insulin coma and tranquillizing drugs—while those with neurotic illness were treated psychotherapeutically and with sedation and modified insulin.

One of the features which has been stressed by previous workers is the occurrence of marked feelings of rejection of the child. This may occur as overt feelings of hatred or disgust, or as a phobia of harming the child. Guilt feelings on this account are thought to be responsible for a high number of suicidal attempts. In this series there was one case of infanticide. One patient complained of having lost her love for the baby and two complained of feelings of wishing to harm the child. Thirteen patients attempted suicide, all but two of these suffering from either endogenous or neurotic depression. In the non-puerperal series there were only two cases of attempted suicide.

At the follow-up interview the patient was asked about her attitude towards the child at that time. Six patients stated that they still blamed the child for the illness and resented its presence. None of the patients blamed the husband for the illness, nor was any antagonism expressed towards him, at least in reference to the pregnancy or the subsequent mental illness.

A follow-up study was carried out on both groups of patients and all but three were traced; of those untraced, one, a schizophrenic, was known to have returned to Ireland and been admitted to a mental hospital there, while no information was available regarding the remaining two, who had left the district. All three patients were in the puerperal mental illness group.

The period of follow-up varied from six months to over five years. Those patients who had not been out of hospital for at least six months are not included in this part of the survey, so that information is available concerning thirty-seven patients in the puerperal group and thirty-nine of the non-puerperal group. The results are shown in Table IX.

As a measure of the severity of the illness in each patient, note has been made of the total number of days spent in hospital, and this is expressed as a percentage of the total period which has elapsed since the date of admission. This gives more information than the duration of the original stay in hospital

TABLE IX
Follow-up Study

	Up to 1 year		Up to 2 years		Up to 3 years		Up to 5 years	
	Puer-peral	Non- neur-peral	Peur-peral	Non- neur-peral	Peur-peral	Non- neur-peral	Peur-peral	Non- neur-peral
Schizophrenia:								
Symptom free ..	5	4	1	1	-	3	1	-
Minor symptoms ..	-	2	1	2	-	-	-	-
Relapse ..	-	-	1	-	-	-	-	-
Readmission ..	-	-	-	-	1	-	1	1
Endogenous depression:								
Symptom free ..	-	-	-	3	1	-	2	1
Minor symptoms ..	1	1	-	1	-	-	1	3
Relapse ..	1	-	1	-	-	1	1	-
Readmission ..	-	-	1	-	-	-	1	-
Neurotic depression:								
Symptom free ..	2	2	2	2	-	-	-	1
Minor symptoms ..	1	2	2	1	-	-	1	1
Relapse ..	-	1	-	1	-	-	-	-
Readmission ..	2	-	-	-	-	-	1	-
Anxiety state:								
Symptom free ..	2	-	1	-	-	-	-	-
Minor symptoms ..	1	3	-	-	-	1	1	-
Relapse ..	-	-	-	1	-	-	-	-
Readmission ..	-	-	-	-	-	-	-	-

since it provides an indication of the total incapacity. It does not, however, take into account the occurrence of symptoms which do not require hospital treatment.

The mean percentage time in hospital of the four diagnostic categories in each group of patients is shown in Table X.

TABLE X
Mean Percentage Time in Hospital

	Puerperal Mental Illness Per cent.	Non-Puerperal Mental Illness Per cent.	t-test
Schizophrenia	20.9	30.6	1.2 NS
Endogenous depression ..	7.2	7.3	Not carried out
Neurotic depression ..	16.4	7.7	
Anxiety state	7.4	10.3	1.6 NS

t-tests show that there is no significant difference between each pair of means; that is, the morbidity rate as measured by percentage time spent in hospital does not differ in the two groups of patients in each diagnostic category.

Table IX shows the number of patient who were re-admitted and also those who had relapsed but were not sufficiently ill to return to hospital. It therefore provides a different measure of the degree of morbidity found in the two groups of patients. Dividing the clinical state at follow-up into two groups instead of four, these being "Symptom-free" and "Minor symptoms only" in one, and "Relapse" and "Re-admission" in the other, a chi-squared test shows there is no significant difference between the two groups of patients ($\chi^2=2.3$; $p>0.1$).

There are insufficient numbers to obtain satisfactory information about the individual diagnostic groups.

An important question in reference to prognosis is the likelihood of further illness in association with further pregnancy. Details are shown in Table XI.

TABLE XI
Relationship Between Further Pregnancy and Breakdown in Puerperal Mentally Ill Group
Further Pregnancy

	With Mental Illness	Without Mental Illness	Further Mental Illness Without Pregnancy
Schizophrenia	0	2	2
Endogenous depression	2	3	0
Neurotic depression	1	0	0
Anxiety state	0	0	0

Of the normal puerperal women, two had had a mental illness in association with a previous puerperium and now showed no sign of recurrence, while two had a history of depressive illness unrelated to pregnancy, one treated by electroplexy; neither of these now showed sign of mental illness.

In the non-puerperal group, one schizophrenic, one endogenous depressive and two neurotic depressive patients had a history of a previous breakdown in association with the puerperium.

DISCUSSION

Two aspects of this study require examination.

The first of these is a consideration of any differences between normal puerperal women and those who develop mental illness. Information is available concerning the incidence of previous psychiatric illness, morbid family history, predisposing personality traits and such stresses as marital difficulties, obstetric complications, unwanted pregnancies and premarital conception. As may be expected, there was a higher incidence of previous psychiatric illness, morbid family history and predisposing personality traits in those patients who developed mental illness. When one considers the number of patients in whom there were considered to be stressful circumstances, whether marital, domestic, social or obstetric, the numbers in the two groups are remarkably equal. Perhaps because the normal patients were seen in a teaching hospital obstetric unit, there is a higher incidence of obstetric complications in this group than in the mentally ill group. The number of children, and the number of previous pregnancies also showed no relationship to the incidence of puerperal mental illness. One must conclude from these findings that the development of puerperal mental illness depends more on hereditary and personality factors than on the immediate stressful events in the patient's life.

The second aspect requiring consideration is the relationship between the patients in whom the mental illness was preceded by parturition and those in whom this was not so. The two groups show many similarities. In both there is a high incidence of previous mental illness, 28.6 per cent. in the puerperal and 14.3 per cent. in the non-puerperal group. Both have a high incidence of morbid family history, 26.2 per cent. and 31.0 per cent. respectively. The immediate prognosis as indicated by the condition on discharge, and the later prognosis shown by follow-up studies also reveal no marked differences.

The main difference between the two groups is shown in the period which elapsed between onset of symptoms and admission to hospital. In the puerperal group 28 patients developed symptoms before the end of the fourth week after parturition and of these, thirteen were admitted to hospital in that period. The majority, 36, of the puerperal patients were in hospital within six months of the onset of symptoms but only 23 of the non-puerperal patients were admitted within six months of the development of symptoms. Since it is generally considered that early treatment, particularly of schizophrenia, is of importance in achieving a satisfactory therapeutic response, the earlier admission should be a favourable feature.

No details are given of individual cases, but there was no evidence of any special features in the clinical state of the puerperal patients to distinguish them from the non-puerperal group except the attitude of the mother towards the child. This may be considered a significant feature distinguishing the condition from non-puerperal illness, but it seems much more reasonable to consider that concern with the recent event of childbirth is a likely pre-occupation of the mother. If therefore, she develops a depressive illness for example, it would be expected that, as in non-puerperal illness, the thought content would be depressive and the pre-occupation would be about the harm she believes she has done, or the fear of doing harm. Phobias of harming children have been seen independent of puerperal illness, though often in association with guilt concerning the child, as for example an illegitimate birth, or even past indiscretions unassociated with the particular child in any way. There is therefore no indication that puerperal illness is in any way a unique illness, but the symptoms and prognosis are in general similar to other types of mental illness. It is schizophrenia which some authors believe has a hopeless prognosis. In this series, of the fifteen cases of post-partum schizophrenia, two were discharged unchanged and three were still in hospital at the time of examination. There were no schizophrenics in the non-puerperal group undischarged and all were considered to have improved. In the follow-up study no information was available on two of the puerperal patients but even if they are assumed to have been re-admitted to other hospitals, five patients had further illness as compared with one non-puerperal schizophrenic. Added to this is the fact that two puerperal schizophrenic patients had had a further child without illness. Therefore one must consider the prognosis to be somewhat guarded in puerperal schizophrenia but not to have the entirely unfavourable outlook suggested by some authors.

Two features which are important for the family as a whole after the distressing occurrence of puerperal illness, are the effect it may have on the mother's attitude to the child and to her husband, and secondly, the likelihood of developing a further illness in association with a subsequent pregnancy. Several patients described marked feelings of rejection of the child while others experienced phobias of harming the child or husband. These latter symptoms have been interpreted as manifestations of similar unconscious feelings of rejection. Tetlow (1955) reports that all his cases of affective psychosis showed this symptom, which may persist for many years. He also stated that in non-puerperal women who described such a symptom, he found evidence of a mild, unnoticed depression that had occurred in association with the birth of the child.

The patient who killed her children, twins, is a paranoid schizophrenic, still in hospital, and maintains that she is fond of her remaining children and expresses regret at the death of the twins. The patients who described overt

feelings of rejection or loss of love for the child had regained their affection at the time of follow-up. Six other patients who had expressed no such symptoms in hospital blamed the child for the illness when seen at follow-up and were still antagonistic towards it.

There was a high incidence of attempted suicide in the puerperal group of patients, and this again has been interpreted as representing an indirect wish to harm the child by withdrawing the source of food. It is more usually considered a result of guilt feelings associated with a depressive thought content. There was no further incidence of suicidal attempt in these patients after recovery from the illness.

Taking these features together, the occurrence of puerperal mental illness leads to great distress in the family and can result in later difficulties for the child as a result of the rejection by the mother, as well as the disturbance which occurs at the time of the illness.

For this reason it is important to be able to assess the likelihood of a further mental illness in association with subsequent pregnancies. Eight pregnancies had occurred by the time the follow-up study was carried out, and three of these patients developed a further mental illness, two having an endogenous depression and one a neurotic depression. The latter patient has a persistent depersonalization syndrome but the two endogenous depressions again responded to electroplexy. Two patients who had suffered from schizophrenic illnesses and three who had endogenous depression became pregnant and were delivered without incident. From these few cases no conclusion can be drawn. It is usually advised that a patient should wait at least two years before considering a further pregnancy, since there is always a possibility of further illness independent of any pregnancy. Two schizophrenic patients developed further illness in this way.

If a patient does become pregnant one has to consider whether to allow the pregnancy to continue or to recommend termination. Each case must be judged individually, with personal history of the patient and type of illness being taken into consideration. One must also bear in mind the findings of Ekblad (1955) that 25 per cent. of his patients developed guilt reactions following abortions induced on psychiatric indications. Arkle (1957) concluded that termination of pregnancy on account of the mental state of the patient is rarely justified by British law since the mental and physical state of the mother is not affected by continuation of the pregnancy. He recognized, however, that social, humanitarian and eugenic aspects are neglected by the law as it now stands.

Summarizing the information presented, the patients who develop puerperal illness differ from normal puerperal women in their hereditary and personality make-up, and are in most respects identical with a group of patients with mental illness not associated with the puerperium. This suggests that the puerperium acts as a precipitating event in a predisposed person. There is no indication as to the way in which the pregnancy or puerperium acts as a stress. No consistent pattern was observed in the genetic or personality structure, nor was there any consistent feature in the pregnancy concerned. However, this is not surprising since we have no real knowledge as to the precise aetiology of many psychiatric illnesses.

Since puerperal mental illness is essentially similar to non-puerperal illness, assessment of prognosis will depend on similar features. Thus a good prognosis in a schizophrenic illness would be associated with acute onset, sound previous personality, and lack of family history and pyknic body build. The acute onset and early treatment are particularly likely to be features of schizophrenia

occurring in the puerperium and one would therefore expect a reasonably good prognosis. It is probably for this reason, the fact that in spite of presence of the usually accepted satisfactory prognostic features, puerperal schizophrenia does not always respond to treatment, that the gloomy prognosis is offered.

If one accepts the suggestion that pregnancy or the puerperium acts as a precipitating stress, one would expect that if an illness occurs after one confinement, it may well do so on a subsequent occasion. Similarly, however, if the illness responded to treatment previously, it is likely to respond a second time. In one's advice concerning further pregnancy, one must bear in mind the possible effects on the whole family of a fairly prolonged period of mental illness, balanced against the probability of eventual recovery.

No information is available as to the way in which the puerperium acts as a stressor, whether it is psychological or physical, or a mixture of these. Such knowledge would be of prophylactic value. It is unlikely that psychotherapy can prevent a psychotic episode but this may be of value in eliminating some of the anxiety states consequent upon parturition. Jacobs (1943) and Boyd (1942) both stress the need for careful psychological management and as Martin (1958) points out, it would seem wise to enquire in early pregnancy about marital stresses and home difficulties which may be alterable.

If a patient is considered to be likely to develop a mental illness after parturition, observation during the puerperium may enable early treatment to be instituted to prevent such distressing complications as suicidal attempts. Further investigation, with a controlled study, is necessary to establish whether investigation during the pregnancy would be of value in identifying patients likely to develop mental illness, and whether support during the pregnancy and puerperium would actually reduce the incidence of mental illness.

In conclusion one can only quote the words of Professor Anderson (1950): "The interest invariably aroused by this topic showed that psychiatrists had not rid themselves of the feeling, illusory though it might be, that the mental illness of the puerperium had unusual features."

SUMMARY

Forty-two patients with puerperal mental illness were compared with a similar number of non-puerperal patients with mental illness, matched for age and illness, and normal puerperal women.

The mentally ill puerperal women differed from the normal puerperals in respect of history of previous illness in themselves and their relatives.

The mentally ill puerperal women did not differ significantly from the mentally ill non-puerperal women.

It was concluded that the puerperium acts as a stress precipitating mental illness in the predisposed woman.

Observation during pregnancy and the puerperium may be of value in reducing the incidence of suicidal attempts and possibly of the mental illness.

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EXPERIMENTAL STUDIES OF THE PLACEBO RESPONSE

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THE critical evaluation of new drugs or remedies against inert substances or non-specific procedures has led to the recognition that responses to a placebo are important in their own right. Such responses may be dramatic and persistent and they can be associated with quite definite physiological changes (Wolf and Pinsky, 1954). The placebo response may well be an important component of many established treatments both physical and psychological, and does in itself constitute a means of therapy (Roberts and Hamilton, 1958; Gliedman *et al.*, 1958).

Most placebo responses have been studied during the course of a clinical trial or hospital treatment. These studies have defined some of the features of the placebo response, and some of the characteristics of the placebo responder. This literature has been reviewed by Trouton (1957). The experiments here reported are an attempt to reproduce similar responses in healthy volunteers under experimental conditions in order to investigate specific aspects of the placebo effect. Our aims were twofold. (1) To assess the effect of varying the conditions of administration upon the number and type of placebo responses and (2) to determine some of the personality correlates of the placebo responder.

The placebo, a small white lactose tablet, was introduced as an active preparation in the following way. "The drug to be administered is a substance which is being tested experimentally in the Research Department. Many effects have been reported following its administration and it will help us greatly to have the benefit of your personal experience."

In all the experiments the placebo response was measured by the subject ticking off one or more of 26 possible drug effects which were listed in alphabetical order on a duplicated form handed to the subject before he was given the placebo. Many of the effects were those described by Beecher (1955) as toxic side-effects of a placebo. The total list could be classified into 13 "pleasant" and 13 "unpleasant" effects. Each subject was asked to tick only those effects which he or she thought were due to the action of the drug; particularly marked effects could be double ticked. Further, the time at which this tick was made was to be recorded.

To assess the effect of varying the conditions under which a placebo is taken the placebo was administered under two conditions, "individual" and "group". Under "individual" conditions each subject sat alone, was given the placebo, and was asked to report on the check list the effects of the "drug" during a 30-minute period. Under "group" conditions three subjects seated together in the same room were similarly asked to report effects. They were unobserved

and free to talk. By administering the placebo to groups of individuals we hoped to produce a situation analogous to that sometimes operating during treatment in hospital wards or out-patient departments.

To determine some of the personality correlates of the placebo responder the subjects were asked to complete the Maudsley Personality Inventory (M.P.I.) (Eysenck, 1959) which gives measures of "neuroticism" and "extraversion" as defined within Eysenck's personality theory. This choice was determined not only by the considerations of ease and speed of administration but also because these measures have been related to aspects of learning and of suggestibility (Eysenck, 1947, 1957), psychological processes thought to be particularly relevant to placebo research (Gliedman, Gantt and Teitelbaum, 1957; Kurland, 1957; Trouton, 1957).

To facilitate presentation, results are reported for experiments carried out under "group" or "individual" conditions rather than in their chronological order. Two of the experiments were under "group" and two under "individual" conditions.

PLACEBO RESPONSES OF SUBJECTS TESTED IN GROUPS

GROUP CONDITIONS: EXPERIMENT I

In the first experiment under "group" conditions 12 subjects, mostly nursing staff (11 of them female) were randomly allocated to four groups of three. Eight of these 12 subjects reported experiencing one or more effects over the thirty-minute period following the administration of the placebo. In all, 28 responses were recorded, 12 (42.9 per cent.) of which were pleasant and 16 (57.1 per cent.) were unpleasant.

When each of the personality measures was correlated with the number of placebo responses (both pleasant and unpleasant) the correlation with neuroticism was highly significant ($r=0.89$, $p=<.01$). The correlation with extraversion, however, was not significantly different from zero ($r=0.20$).

To confirm this finding of a close association between neuroticism and placebo responding, a further four groups were tested under "group" conditions.

GROUP CONDITIONS: EXPERIMENT II

A group of 13 hospital nurses who had volunteered to participate in this study were ranked in order of their neuroticism scores. Initially subjects 2-13 were then placed in four groups of three by taking successive numbers. Our intention was to obtain four groups which could be ranked in order of their mean neuroticism scores, the prediction being that the total number of placebo responses recorded for each group would show an identical rank order. However, because of conflicting duty hours we were unable to maintain these original groupings. This had two unfortunate effects. Firstly, two of our groups had mean neuroticism scores which were almost identical and secondly, the previous balance of extraversion scores was upset. In view of the unsatisfactory grouping the data were analysed by correlating scores on neuroticism and extraversion and the total number of placebo responses recorded by each of the 12 subjects. The correlation with neuroticism is again positive ($r=0.37$) although significantly lower than that previously found. The correlation with extraversion on this occasion is significant ($r=0.69$, $p=<.05$).

Three of the groups gave 25 responses between them, the fourth group failed to respond at all. The behaviour of this fourth group was strikingly different to that previously experienced and we believe that this failure to

respond may perhaps be accounted for by the behaviour of two student nurses being inhibited by the presence of a ward sister who was the third member of the group. The lack of response in this group had the effect of diminishing the correlation with neuroticism and of slightly increasing the correlation with extraversion. When this fact is allowed for the correlations for the remaining 9 cases are 0.52 and 0.66 for neuroticism and extraversion respectively.

Since in these two experiments the subjects and conditions of administration are relatively constant, the correlations between the personality factors and the number of placebo responses have been combined to give the best estimate of these correlations under "group" conditions of administration. The correlations show a close relationship between neuroticism and placebo responding under "group" conditions ($r=0.65$, $p<0.01$). On the other hand, there appears to be little association with extraversion ($r=0.38$, $p>0.05$). When the atypical group in the second experiment is omitted from the calculations the correlation with neuroticism is increased to 0.74, the correlation with extraversion remains unchanged.

An alternative way of expressing the relationship between neuroticism and placebo responding is shown in Figure 1. The regression line giving the best prediction of the number of placebo responses given scores on neuroticism was calculated from the data of both experiments. In view of the uncharacteristic

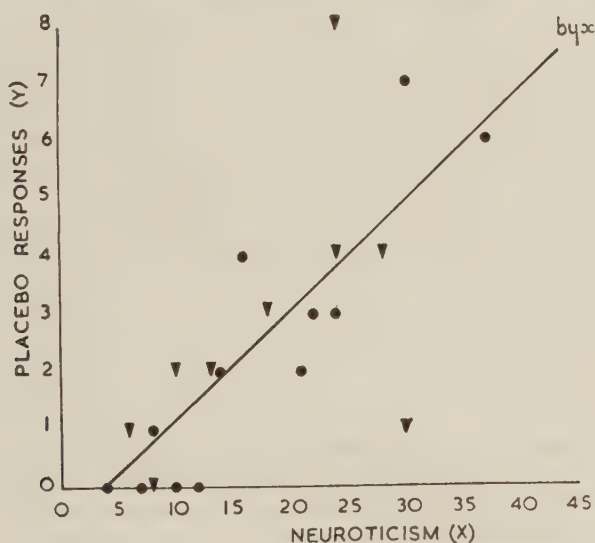


FIG. 1.—Placebo responses under "group conditions" plotted against scores on neuroticism with the regression line calculated from these data. ($n=21$.)

● = Experiment 1.

▼ = Experiment 2.

behaviour of one of the groups in Experiment II, it seemed justifiable to omit them from this calculation and from Figure 1. The number of placebo responses given by the remaining 21 subjects in our two experiments have been plotted against their scores on neuroticism. It can be seen from Figure 1 that there is little scatter about the regression line and that the subjects in both experiments are alike in this respect.

In conclusion, it would appear from our two experiments that when subjects are seated together in a group, neuroticism, but not extraversion, has a close association with the degree of response to a placebo.

PLACEBO RESPONSES OF SUBJECTS TESTED INDIVIDUALLY

Whereas in the two previous experiments the subjects were seated in groups during the thirty-minute observation period, in the two experiments to be reported now, the individuals were asked to record effects whilst sitting alone.

INDIVIDUAL CONDITIONS: EXPERIMENT I

Eleven subjects (7 of them female), mostly nursing staff, were used in the first of these experiments. Each completed the M.P.I. and was introduced to the placebo in the manner previously described.

Seven of our 11 subjects reported experiencing one or more "drug" effects. These seven subjects gave 27 responses between them; this figure is almost identical to those previously reported under group conditions. Thus, changing the conditions of administration apparently made no difference to the total number of placebo responses recorded. However, whereas under "group" conditions pleasant and unpleasant effects are almost equally represented in this experiment, pleasant effects predominated significantly (81.5 per cent., $p = < .002$).

The correlations between the personality factors and the total number of placebo responses show striking deviations from those reported under "group" conditions. The correlation with extraversion is positive and significant ($r = .63$, $p = < .05$), but the correlation with neuroticism is virtually zero ($r = .07$).

The predominance of pleasant effects recorded in the record sheets of the subjects, and the high correlation with extraversion, suggested to us the hypothesis that this correlation was a function of differences in "set" between introverts and extraverts; the extraverts being more prone to attribute relatively normal changes in mood, etc., to the action of the "drug".

This hypothesis was tested in a second experiment. This also provided an opportunity to confirm our findings regarding the neuroticism factor.

INDIVIDUAL CONDITIONS: EXPERIMENT II

The design of this experiment was based on the observation that introverts "carry out tasks slowly but accurately" whilst extraverts "tend to do them quickly and inaccurately" (Eysenck, 1946). It was postulated that accuracy in observing subjective changes and, therefore, in discriminating them from drug effects, would be an attribute of introverts, whilst for extraverts the converse would be true. However, by stressing the importance of accuracy in our instructions to the subjects it was thought that the set that the introvert adopted as a matter of course could be imposed upon the extravert. In other words, if such instructions brought about a homogeneity in set, then the number of reported placebo effects should be the same for both introverts and extraverts under these conditions.

Procedure

The placebo effect was measured after two types of instructions had been given. The first was comparable to that given in the first experiment; the subject was merely asked to report effects that he thought were attributable to the drug ("no stress" conditions). The second opened with a statement to the effect that the experiments were highly important and crucial; and the importance of accurate reporting was stressed throughout ("stress" conditions).

In testing this hypothesis four groups of theological students were taken from a group of 46 according to whether or not they scored high or low on the E factor. There were two matched groups of introverts and two matched groups of extraverts; the mean E scores were approximately 16 and 31 respectively. Analysis of variance indicated no significant differences in neuroticism between these four groups. One group of introverts and one group of extraverts were tested under "no stress" conditions, the other groups being tested under "stress" conditions. The allocation of "stress" and "no stress" conditions to the groups and the order of testing was random.

Specifically the predictions were:

- (a) That under "no stress" conditions the extraverts would give a significantly greater number of placebo responses than the introverts: a prediction based upon our earlier finding.
- (b) That under "stress" conditions the extraverts would show a significant reduction in the number of responses (the effect of set) whereas the introverts would remain relatively stable.

Results

The results (Table I) have been analysed by non-parametric techniques (Siegel, 1956). The introverts under "no stress" conditions give more responses than do the extraverts, but this difference was shown to be insignificant by the Mann-Whitney U Test ($U=7.0$, $p=.09$). Under stressed conditions there are more responses and the two personality groups behave alike. From the data it appeared that there could be an interaction between personality and type of instruction, i.e. the extraverts tending to respond more when accuracy was stressed. Thus there is no support for either of our predictions.

To test the significance of the observed interaction, difference scores were obtained by noting the discrepancies in scores for the matched pairs under the two experimental conditions. These two sets of scores were then compared by means of the Mann-Whitney U Test; this test indicated no significant difference ($U=14.5$, $p > .5$) and thus there is no real difference in the change of score between the two groups.

TABLE I

The Total Number of Placebo Responses Given by the Extraverted and Introverted Groups Under the Two Experimental Conditions

	Extraverts		Introverts	
	No Stress N=6	Stress N=6	No Stress N=6	Stress N=6
No. of placebo responses ..	3.0	19.0	12.0	17.0

In view of this finding the scores for introverts and extraverts were combined to see whether there was a significant increase in scores when the instructions were altered. Wilcoxon's matched-pairs signed-ranks test showed this increase just failed to reach significance at the 5 per cent. level ($p=.07$).

This increase in score probably reflects an increase in interest in the experiment, an interpretation similar to that given by Glaser (1953) who found that when three drugs and a dummy were given in random order at seven-day intervals, questionnaire responses gradually declined until the fourth and last administration when there was a significant increase.

The correlations between personality and placebo measures were computed for the "no stress" conditions. The correlation with neuroticism is again found to be positive but low and insignificant ($r=0.17$); this confirms our earlier finding for individuals. The correlation with extraversion is, however, negative ($r=-0.39$) rather than positive as in our previous study, although with this size of sample it does not reach statistical significance.

SUMMARY OF FINDINGS, AND CONCLUSIONS

The experimental procedures enabled us (1) to compare the number and type of placebo responses, and (2) to determine some of the personality correlates of the placebo responder under the two conditions of administration, "group" and "individual".

Regarding the first of these we have found that the total number of placebo responses under the two kinds of administration are remarkably uniform (Table II). The only exception is the second experiment under "individual" conditions where it has already been noted that instructions stressing the importance of the experiments and accurate reporting markedly increased the placebo scores of the students. Again except in one case (Experiment I, "individual" conditions) the number of pleasant effects reported is approximately equal to the number of unpleasant effects under both "group" and "individual" conditions. We conclude, therefore, that varying the conditions of administration as between "individual" and "group" makes no difference to the number or type of placebo responses.

TABLE II

Total Number of Placebo Responses Classified as "Pleasant" (P) or "Unpleasant" (U) in Each of the Four Experiments

Experiment	Placebo Responses		Group Administration				Individual Administration					
			Experiment I		Experiment II		Experiment I		Experiment II			
			N=12		N=12		N=13		No Stress N=12		Stress N=12	
Type	..		P	U	P	U	P	U	P	U	P	U
Number	..		12	16	13	12	22	5	8	7	18	18
Total	..		28		25		27		(Mean=25.5)			

Concerning the personality correlates of the placebo responder some interesting findings have emerged (Table III).

TABLE III

Correlations Between Total Numbers of Placebo Responses and Neuroticism and Extraversion Under Group (Combined Data) and Individual Conditions

Administration				Neuroticism	Extraversion
Group: N=21	..	..	..	0.74*	0.38
Individual: N=11	..	..	..	0.07	0.63†
	N=12	..	..	0.17	-0.39

* $p < .01$ † $p < .05$.

It would appear from our experiments that the relationship between personality dimensions and placebo responses is to some extent dependent upon the conditions under which the placebo is administered. This interpretation is clearest for neuroticism; under "group" conditions the correlation is highly

significant but under “individual” conditions the correlation is not significantly different from zero. The finding for extraversion is less clear-cut. Under “group” conditions the overall correlation is positive but does not reach significance. Under “individual” conditions, that is, when the individuals were tested in isolation, we obtained contrary findings. When the subjects were nurses the correlation was positive and significant; when they were theological students the correlation was negative but insignificant. A possible explanation for these discrepant results is discussed below.

The actual findings in terms of symptoms reported are detailed on the symptom check list which is reproduced below.

The Symptom Check List together with the Number of Times each Effect was Reported by the Subjects in all Four Experiments (N=59)

Symptoms		Symptoms	
Able to see more clearly ..	0	Energetic	2
Able to think more clearly	3	Gay	7
Aches and/or pains ..	7	Less tired .. .	8
Agitated	2	Lethargic	6
Alert	4	More comfortable ..	2
Apprehensive	2	More tired	7
Attentive	3	Confused thinking ..	5
Calm	11	Blurred vision	4
Clearheaded	6	Pleasantly detached ..	3
“Couldn’t care less” ..	4	Relaxed	20
Depressed	0	Restless	3
Distractable	0	Strange and unreal ..	3
Drowsy	12	Thick headed	7
			131

Information regarding the distribution of scores on neuroticism and extraversion for the four experimental groups for which correlation coefficients were calculated is given below in Table IV.

TABLE IV
The Mean Scores and Standard Deviation for Neuroticism and Extraversion for the Experimental Groups Under the Two Conditions of Administration for which Correlation Coefficients have been Calculated

Experiment	Neuroticism		Extraversion	
	Mean	S.D.	Mean	S.D.
Individual conditions:				
Experiment I (N=11)	.. 19.82	9.45	28.27	7.52
Experiment II (N=12)	.. 25.83	11.92	24.00	9.29
Group conditions:				
Experiment I (N=12)	.. 17.08	9.97	27.42	11.31
Experiment II (N=12)	.. 18.42	7.79	28.50	7.45

DISCUSSION

Following administration of a placebo 66 per cent. of our 59 subjects reported experiencing one or more effects which they attributed to the action of a “drug”. This high figure, similar to that previously reported by Glaser and

Whittow (1953) indicates that we were successful in our attempt to reproduce a placebo effect under experimental conditions. Whether or not the placebo responses we described are analogous to those under clinical conditions has yet to be shown, and thus it would be unwise to generalize from our selected populations. There are obvious and no doubt important differences between nurses and students volunteering for experiments with new "drugs" and patients seeking relief from often debilitating symptoms. The similarities are, however, no less clear; effects attributed to an active substance are experienced, despite the absence of any pharmacological action.

Many of the reported effects were mild, for example, feeling "relaxed", "calm", "drowsy". Some, however, were quite striking. One theological student complained of pain on the top of his head which radiated on to his face and lower jaw. One nurse complained of extreme nausea and developed a marked pallor; another noted marked blurring of vision.

Many writers have loosely attributed the placebo effect to "suggestibility". Such statements, however, are of little value unless suggestibility itself is clearly defined, for Eysenck and Furneaux (1945) and Stukart (1958) have shown that tests commonly employed to measure this attribute can be referred to more than one factor after factor analysis. Eysenck's original description of primary (or ideo-motor) suggestibility (Eysenck, 1943) has recently been confirmed by Stukart (1958) who also expanded the concept of secondary suggestibility of Eysenck and Furneaux (1945) in a way particularly relevant to our own study.

This factor of secondary suggestibility is characterized by the influence of such subjective factors as expectation or "set", and the need for conformity upon the individual's perceptions, memory, and judgments. Further, Stukart showed that neurotics were more suggestible when tests of this type were employed. In these cases the suggestion was not only of the "indirect" kind (Eysenck and Furneaux, 1945) but came also from the personal pressure of the examiner and from rehearsed co-judges. This finding confirmed his hypothesis that "neurotics are more suggestible than normals in situations where an element of personal pressure, activating the need for conformity of the subjects, is inherent in the suggestions . . ." (*op. cit.*, p. 124).

In our studies on groups such personal pressure could have come both from the direct suggestion of the experimenter that the inert tablet was a drug under investigation, and from other members of the group whenever they made a response. We found that in many cases there was a marked concordance in the times at which identical or similar "symptoms" were noted by different members of the group, a finding which strongly supports this interpretation.

Joyce (1959) found with healthy medical students working in pairs, that placebo responders were, among other things, "more sensitive to social influences", and more particularly, were found to be less "dominant" and less "self-confident" on the Bernreuter Scale. He also found evidence for emotional lability in the reactor group as shown by greater variability in pulse rate. From the known inter-correlations of the individual Bernreuter scales (*cf.* Vernon, 1953) Joyce's results indicate higher neuroticism of the reactors, a finding in agreement with our own for groups.

Our finding that there is virtually no correlation with neuroticism under "individual" conditions is not necessarily inconsistent with the above argument, for under these conditions the personal suggestions were restricted to the opening remarks of the experimenter. The low and insignificant correlation between neuroticism and placebo responding was found on both occasions when the subjects, nurses and theological students, were tested individually.

This finding needs to be confirmed with patients before its implications are fully explored. However, accepting the evidence as it stands the effect of a placebo on a neurotic population is likely to be enhanced if the person treated is one of a group attending an active out-patient department. For example, the high level of placebo response obtained by Hawkins and Tibbetts in their trials of acetylcholine and carbon-dioxide therapy (1956a, b) were obtained in a setting of which particular features were social mixing before and after treatment and the presence of a high proportion of patients receiving benefit from E.C.T. giving rise to "high group morale and a great sense of therapeutic optimism".

Under "individual" conditions our results showed that the correlation with the extraversion factor was positive for nurses but negative for the theological students. A possible explanation is that on account of their different background and their consequent lack of sophistication in regard to drug effects, the theological students could not discriminate as clearly as could nurses between spontaneous changes in mood and sensation, and likely drug effects. The student who wished to be accurate (our hypothesis was that such a set characterized the introvert) would therefore, attribute these changes to the action of the drug. In contradistinction the nurse who also wished to be accurate would discount them.

It is possible, therefore, that personality factors operate against a background of knowledge and experience, and that where this is different, responses that are apparently contradictory in their relation to personality dimensions may occur. This hypothesis obviously requires confirmation, but it is probably in accordance with findings such as Lasagna's. He found marked differences in attitude—presumably a reflection of experience—between his placebo responders and non-responders (Lasagna *et al.*, 1954).

SUMMARY

Four experiments are reported in which the effect of a placebo in healthy subjects has been studied. The placebo was a small white lactose tablet which was administered orally and introduced as a drug with potential effects. For thirty minutes following the administration of the placebo the subjects recorded symptoms on a check list of 26 items, half of which were pleasant and half unpleasant.

In two of the experiments the subjects spent the thirty-minute observation period sitting alone (individual conditions) and in the other two, subjects were seated in groups of three (group conditions).

Before each experiment all the subjects completed the M.P.I.

Sixty-six per cent. of the subjects ($N=59$) reported one or more effects. Analysis of the data led to the following conclusions:

1. The total number of responses reported remained constant despite altering the conditions of administration (i.e. "individual" and "group").
2. The proportion of pleasant to unpleasant responses remained approximately one-half throughout the experiments.
3. The relationship between placebo responding and personality varied according to the conditions of administration. This was clearest for neuroticism where the correlation was high ($r=.74$) under "group" but insignificant under "individual" conditions.

The interpretation of the correlations with extraversion was less clear. When homogeneous samples were tested the pattern of correlations was the converse for

that of neuroticism, i.e. significant correlation under "individual" but insignificant under "group" conditions. However, when theological students, as opposed to nurses, were tested, the correlation became negative. A possible explanation was discussed.

4. "Stress" administration in which the importance of the research and the necessity for accurate observations were emphasized, increased responses.

The findings, and their relation to those previously reported, were discussed in detail.

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SPECIFICITY OF IMMEDIATE MEMORY FUNCTION ASSOCIATED WITH CEREBRAL CORTEX DAMAGE*

By

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THE psychometric assessment of memory presents special problems in that inferences regarding this function seem to be markedly dependent upon the conditions under which it is measured. Thus, following exposure to experience X, it is problematic whether a single statement regarding a person's ability to remember X can be made. His ability would likely be a function of the time between exposure and reinstatement (Ebbinghaus, 1913; Luh, 1922; Postman and Rau, 1957) and whether assessment involved recognition, free recall, or relearning (Luh, 1922; Postman and Rau, 1957). Beyond these, the importance of the sensory channel involved in the initial experience or in reinstatement (Thurstone, 1938, p. 86) and the nature of the content to be retained (Benton, 1945) remains relatively unexplored. All of these considerations dictate against accepting differing psychological test measures of memory as equivalent and, conversely, suggest that any generalized statements regarding memory ability should be based upon several different measures.

When memory tests are used to aid in the detection of cerebral pathology or to assess the psychological effects of cerebral trauma, still another complicating feature is added. There is an increasing body of research suggesting differential and rather specific decline in psychological abilities associated with lesions of the left and the right cerebral hemispheres. Left hemisphere pathology in right-handed persons is characterized by differential impairment on verbal tasks (Anderson, 1951; Heilbrun, 1956; McFie and Piercy, 1952; Meyer and Jones, 1957; Reitan, 1955). There is considerable evidence that right hemisphere lesions in right-handed persons are associated with a disability on spatial tasks (Brain, 1941; Hécaen, de Ajuriaguerra and Massonnet, 1951; McFie, Piercy and Zangwill, 1950; Paterson and Zangwill, 1944; Paterson and Zangwill, 1945), and some evidence that right-sided pathology is differentially related to spatial impairment (Heilbrun, in press; McFie and Piercy, 1952). Accordingly, the nature of the content of any given memory test could assume a major role in assessment of brain-damaged patients since, for example, an examiner might make a far different inference regarding memory function of a patient with left hemisphere damage if he administered a "non-verbal" memory-for-designs test rather than a verbal retention test.

The view that clinical appraisal of memory in the brain-damaged should not be based on a single memory test was proposed some time ago by Benton (1945), but since that time there has been little evidence reported regarding the degree of relationship between various memory tests in either a brain-damaged or non-brain-damaged population. It is the purpose of this study to determine

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the inter-relationships between several immediate memory tests and to further evaluate whether these inter-relationships differ in a brain-damaged group based on the notion that specific disabilities in dealing with verbal and spatial test content following left and right hemisphere damage could produce specific decline on memory tests with these content characteristics. Such data will provide direct evidence as to whether a general statement regarding a brain-damaged patient's memory *ability* is permissible or whether several statements regarding memory *abilities* are in order (i.e. whether a single or multiple memory tests are necessary to appraise memory function).

PROCEDURE

Subjects

The 110 patients included in the brain-damaged group were judged to have lesions involving the cerebral hemispheres and were collected from the neurological services of the State University of Iowa Hospital and Veterans Administration Hospital, Iowa City. The 68 patients in the non-brain-damaged group were obtained from various non-neurologic wards of the same hospitals and included patients with no history or current suspicion of brain pathology. The groups were matched for mean age (brain-damaged, 41.8 years; controls, 41.1 years) and mean educational level (brain-damaged, 9.8 years; controls, 10.1 years).

Memory Tests

The four immediate memory tests selected for this study were chosen because they included divergent characteristics presumed to influence the ability to reinstate previous experiences. They were administered as part of a larger battery of tests, always appearing in the same order relative to each other. These were:

1. The Digit Span Test. This task, a subtest from the Wechsler-Bellevue Intelligence Scale (Wechsler, 1944), required the patient to *recall* series of numbers both forward and backwards. The sensory modality involved was *auditory*, the content *verbal-symbolic*, and the motor act was *vocal*.
2. Visual Retention Test, Form C (Benton, 1955). In this test the patient was *visually* presented *meaningful geometric designs* and was asked to *recall* the designs by *drawing* them.
3. Visual Retention Test, Form G (Benton, 1955). Form G involved the same *visual* presentation of *meaningful geometric designs* (which differed from those in Form C), but the patient was only required to *recognize* the correct design from a multiple choice of 4. Either a *verbal* or *pointing* response was accepted.
4. Serial Synthesis. This task included the *visual* presentation of parts of *meaningless geometric designs* one at a time, and the *recognition* of the combined design from a multiple choice of 4. Again either a *verbal* or *pointing* response from the patient was possible.

The 4 measures were all presented under immediate memory conditions so time between exposure and reinstatement of the stimulus was not a differential characteristic of the tasks.

RESULTS AND COMMENT

The relationships between the 4 memory tasks were analysed by means of product-moment correlations. These correlations for the non-brain-damaged

group are presented in Table I. All of the correlations differed significantly

TABLE I

Correlations Between Performances of Non-Brain-Damaged Patients on Four Tests of Immediate Memory

	Visual Retention Test (C)	Visual Retention Test (G)	Serial Synthesis
Digit span	.42	.35	.50
Visual retention test (C)		.46	.62
Visual retention test (G)			.53

from zero at the 1 per cent. level of confidence. Two inferences may be made from these data. One is that since performance on each test is significantly related to performance on all others, a case can be made for a general memory ability which to some extent governs performance on memory measures of widely varying characteristics. The other inference would be that despite the possible general memory factor, attempts to predict how a patient will perform on one memory task based upon his performance on another will lead to considerable error. For example, the correlations* obtained with the control group suggest that only 12-38 per cent. of the variability in memory scores on any one test can be accounted for by the variability on any other.

The correlations between the memory tests for the brain-damaged group are given in Table II. All of these correlations were reliably greater than zero at

TABLE II

Correlations Between Performances of Brain-Damaged Patients on Four Tests of Immediate Memory

	Visual Retention Test (C)	Visual Retention Test (G)	Serial Synthesis
Digit span	.26	.35	.40
Visual retention test (C)		.61	.49
Visual retention test (G)			.47

the 1 per cent. confidence level except that between Digit Span and Visual Retention Test (C) which reached the 5 per cent. level. Each of these correlations was compared statistically with its counterpart obtained from the control group, and it was found that none of the comparisons provided a statistically significant difference. Thus these between-group comparisons give no support to the notion that *greater* caution is necessary in making test-based statements about general memory ability when dealing with brain-damaged patients than with non-brain-damaged patients. However, it is clear that the *same* limitations regarding any general statement of memory ability from a single test suggested with reference to the control group would hold for the organic group. That is, the correlations between performances of brain-damaged patients on several memory tests suggest that one can account for only between 7 per cent. and 37 per cent. of the variability in scores on any one test from the variability on any other.

* One of the ways in which a correlation can be interpreted is in terms of common variance between the 2 sets of scores which are correlated. Thus by squaring the obtained correlation, the per cent. of common variance can be estimated. As a perfect correlation of 1.00 is approached, the amount of variability in scores on one measure which can be accounted for by the variability on the other approaches 100 per cent. As an example from Table I, the Digit Span-Serial Synthesis correlation of .50 suggests that there is a 25 per cent. common variance and 75 per cent. error variance.

Inspection of the magnitude of correlations when the *verbal* Digit Span performance of a patient was related to his own performance on the three tests with *geometric-spatial* content suggests that differences in the nature of the content may contribute substantially to the limited relationships between memory tests for *both* the brain-damaged and non-brain-damaged groups. The 3 correlations between Digit Span and the memory tests with spatial content for the brain-damaged group (r 's = .26, .35, .40) are considerably lower than the 3 correlations involving only tests with spatial content (r 's = .47, .49, .61). The same trend can be observed in the matrix of correlations based on non-brain-damaged patient performance though it is not so clear-cut (Digit Span vs. spatial; r 's = .35, .42, .50; spatial vs. spatial; r 's = .46, .53, .62). Caution is necessary in this type of inspectional comparison since no statistical safeguards are provided, but it is possible that the larger discrepancies for the brain-damaged group between the set of correlations relating tests with verbal and spatial content as opposed to correlations relating tests with only spatial content do reflect the effects of specific disabilities following laterally localized cerebral trauma. A large group made up of only cases with lesions restricted to a single hemisphere would be necessary to test the hypothesis in a precise fashion.

The importance of these findings to the neurologist would seem to be in the re-emphasis upon the limited statements regarding immediate memory function which can be made should the neurologic examination include a single test of that function. Two options present themselves: (1) increase and diversify the memory measures so that a more comprehensive estimate of memory potential is possible, or, (2) limit the estimate of retentive capacity to the particular operations involved in the single measure. Accepting the second option, the clinician using the Digit Span procedure, for example, might state that a given patient when presented numbers to remember performed at such-and-such a level. Thus any statements are confined to the recall of verbal symbols at most and the diagnostic or prognostic significance is rather limited. However, when performance on several tests of memory are available for a given patient along with useful norms, the clinician has a better opportunity to detect a pervasive, a well-circumscribed, or no disability in memory function. Such observations would more likely have important diagnostic or prognostic implications.

SUMMARY

The measurement of immediate memory skills by psychological tests is complicated by the fact that such tests vary with respect to the nature of the content, sensory modality carrying the test stimuli, whether recall or recognition is demanded, and the type of response which is scored. The present study concerned itself with the degree of relationship between several immediate memory tests which varied with respect to these characteristics. More specifically, the study addressed itself to whether the specificity of loss observed in cases of cerebral cortex damage (e.g. loss in verbal skills following left hemisphere injury; loss in spatial skills following right hemisphere injury) might lead to a lower degree of relationship when memory testing is done with brain-damaged patients.

All intercorrelations between the four immediate memory tests were significant for both control and brain-damaged groups suggesting the operation of a general memory factor. However, they were of such restricted magnitudes as

to indicate considerable caution in drawing any conclusions about a patient's memory functioning from a single test. There were no significant differences in correlations when those for the brain-damaged group were compared with the correlations for controls suggesting that differential impairment on verbal and spatial tasks associated with left and right cerebral lesions does not produce any substantial specific decline in memory test scores when a large unselected group of brain-damaged patients is considered. Implications for the neurologic examination were discussed.

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SCHIZOPHRENIC SYMPTOMS AND CEREBRAL PATHOLOGY

By

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THE illness which was first described by Kraepelin and which he called dementia praecox was more correctly designated as a *Zerfallskrankheit* (disintegrative illness) by Eugen Bleuler, who called the illness schizophrenia. In this disease, or rather group of diseases, not only does one find characteristic symptoms and symptoms which occur in other functional psychoses, but, if suitable methods of examination are employed, symptoms which are found in gross brain diseases, especially those associated with focal lesions, are also elicited. Apart from this, many other symptoms acquire a new aspect when viewed from the standpoint of neuropathology. This may justify our attempt to consider all schizophrenic symptomatology from the point of view of neuropathology. I attempted to do this in my "Report on Cerebral Pathology and its Importance for Neurology and Psychiatry" which I delivered 21 years ago at the annual meeting of the Association of German Neurologists and Psychiatrists at Frankfort-on-Main. Not much space was devoted to the problem of schizophrenia in this report. However, since that time more neuropathological knowledge has been acquired as a result of the Second World War, and this has added to the not inconsiderable knowledge of neuropathology which we already had in 1936 as a result of the First World War. The increasing number of brain injuries due to road accidents has also increased our knowledge of neuropathology. New approaches to the schizophrenic syndromes have been made possible by this growth of our knowledge of the effects of brain injury. Apart from this, I was able, in collaboration with Professor Leonhard and others, to finish a few years ago the clinical follow-up studies on schizophrenia which I began in 1936. In this work we encountered a large number of schizophrenic symptoms which had neurological characteristics.

In a Senckenberg Lecture in 1947, I made a review of "Progress in Psychiatry" as I had experienced it in the previous fifty years. On this occasion I felt justified in saying that intellectual processes of deterioration, which are related to the cortex and to various psychiatric brain stem disorders, occur in schizophrenia and that these changes are comparable with those of Huntington's Chorea and Alzheimer's Disease. Both kinds of process act together and produce the affective, psychomotor, delusional, speech confused and thought confused forms of illness which belong to the different groups of hebephrenic, catatonic, paranoid, and confused schizophrenia.

These groups and their subforms can be arranged so that the forms which come first are those which have symptoms with marked neurological characteristics. On the left one can place the forms in which cortical symptoms predominate, while on the right are those forms which are apparently caused by brain stem disorders. By brain stem I mean all the forebrain ganglia, the diencephalon, the mesencephalon and the metencephalon.

This review is confined to the basic forms of schizophrenic illness. Most of these are simple forms, have the same features throughout the course of the illness, progress only gradually and run a course which is that of a "psychiatric system illness". The combined forms which are also systematic will not be dealt with here. Those forms which have been worked out by Leonhard and which develop unsystematically and extensively during the course of the illness will also not be discussed with the exception of those which begin with a characteristic clinical picture. These last forms are distinguished from the systematic forms in our scheme by a punctate underlining.

In order to prevent misunderstanding it must be pointed out that I consider that the general relation between mental phenomena and cerebral processes is merely one of correspondence. So that I am very far from identifying one with the other or from making the psyche into something material. Here I would like to refer to my article on "Brain and Psyche" (13) and earlier statements of a similar kind. When I talk of mental phenomena and processes I am referring to their general nature and not to the special contents in an individual case. It does not matter whether the patient hears the hallucinatory voices of his wife or of his former mistress nor if some current hostility or some past unresolved psychological conflict, of which he is not fully aware, is playing a part in his delusion. The content of a particular stereotypy may be explained as derived from some experience of the patient but not the stereotyped behaviour *per se*.

I. CONFUSED SCHIZOPHRENIAS

1. A patient with this sub-form of schizophrenia (which corresponds with Kraepelin's *Sprachverwirrtheit* (speech-confusion)) described the "broken window-pane picture" (from the Binet-Bobertag collection), which shows a coloured picture of a boy who has smashed a window and a man who gets hold of another boy by mistake, as follows: "Das Bild, das etwas Farbenauftrag braun, gelb, grün, blau, rosa und violett zeigt, ist mit Teefarbenausführung zu bezeichnende Schneewirtschaft. Sein Zeitstil ist das verlassene Mittelalter. Dem Bilde traue ich eine Aufstellung zu und sehe, dass der grünste Junge bereits die Scheibe zerschmettert haben darf." The approximate translation would be: "The picture, which shows some application of colour brown, yellow, green, blue, rose and violet, is with tea colour performance to be designated snow household. Its style is deserted Mediaeval. I credit the picture with a setting-up and see that the greenest boy already may have broken the pane." The second part of the first sentence "ist mit Teefarbenausführung zu bezeichnende Schneewirtschaft" (is with teacolour application to be designated snow household), is paragrammatical. Equally paragrammatical is "haben darf" (may have) instead of "haben dürfte" (might have). Verbal paraphasias are to be found in "das verlassene" (deserted) instead of "das vergangene" (past) and "traue ich . . . zu" (I credit) instead of "vermute ich" (I suppose). "Aufstellung" is agrammatical and stands for: "Ich vermute, dass—eine Bretterwand—aufgestellt ist." (I suppose that—a partition of boards—has been set up.) "der grünste Junge" (the greenest boy) is a faulty word derivation and in the same way the new word construction "Teefarbenausführung" (tea colour performance) and "Schneewirtschaft" (snow household) are just as incorrect. Another patient was looking for words, trying to correct her faulty speech, and finally said that she noticed her own lack of speech understanding, "Ich fühle das auch, dass

die Aussprache gegenseitig schwer gegeben ist." (I also feel that the discussion is made mutually with difficulty.) This is again a paragrammatical misconception.

Understanding and linguistic formulation of abstract and insignificant thoughts, which are themselves markedly connected with speech, are affected the most. One patient had to explain the proverb "Morgenstund hat Gold im Mund". (The morning hour has gold in its mouth, i.e. the early bird catches the worm.) Answer: "Das ist die Taschenuhr . . . ganz sicher . . . vier Gedanken gestrige . . . also vier Uhr." (This is the watch . . . quite sure . . . four thoughts yesterday . . . thus four o'clock.) Only parts of the proverb have been understood, and the sense of it is formulated in a faulty way. Perhaps the patient wanted to say "This means getting up early . . . at four o'clock, as one has planned yesterday . . . therefore one needs the watch." (Das bedeutet früh aufstehen . . . um 4 Uhr, wie man sich gestern vorgenommen hat . . . dazu braucht man die Taschenuhr.)

We are therefore dealing with *sensory aphasic impairments* similar to those found in focal brain lesions of the *left temporal lobe*. The only difference is the involvement in schizophrenia of higher levels of speech which are responsible for word derivations, word constructions, the formation of sentences, and for the abstract meaning of speech conceptions—i.e. the thinking based on speech. On the other hand in focal brain lesions the lower levels of speech, i.e. the sounds, words (sound sequences) and names, are disturbed.

Many years ago, in systematic investigations, my former associate Fleischhacker (4) demonstrated finer disorders of speech understanding in schizophrenics, and Benary and Pittrich (20) were able to detect disorders of speech-based thought in wounded soldiers of the two World Wars.

Vogt and Beheim (22) found cell degenerations, especially atrophic cells (Schwundzellen), widespread in the cerebral cortex of schizophrenics, also in the temporal lobe.

2. In *Paralogical Schizophrenia* the paralogical impairment of comprehending thought is a leading symptom. One of our patients did not recognize the picture of the "Fensterpromenade" (a man greeting two ladies at a window and stumbling over a boy whom he has knocked over), and produced the following paralogical mistakes in thought: "The boy who has fallen down was perplexed at the arriving visitor, or he is ill and has suffered a fit. According to his mien the arriving gentleman is asking for help for the fallen child."

This thought disorder is very close to an *ideational agnosia* as described by Liepmann in focal lesions of the occipital lobe. In defining the concept of a locomotive another patient referred only to a part of this image, "A locomotive is a black chimney". One patient discriminated a child from a dwarf in the following way, "A child is a crazy dwarf, a dwarf is the spirit of the child". Difference is mistaken here for similarity, and the contents of the answer are mixed-up concepts. Maybe he had in his mind: The dwarf is different from the child in that he is "crazy" (i.e. malformed), but has as normal a spirit as the child.

When asked about the meaning of the proverb, "Hunger ist der beste Koch" (Hunger is the best cook) he said, "When you are hungry you prepare the meal yourself". Obviously putting himself into the situation of the proverb the patient took as the best cook the man who always knows how

to look after himself, according to the proverb "Selbst ist der Mann" (One does things best oneself). This shows a mingling of concepts. The same patient talked one day about water from a "Wiesenbach" (meadow-stream) and continued, "... aus dem Jesubach, dem Bach, der über Jesus geschrieben hat" (. . . from the Jesu-Bach, the Bach, who has written about Jesus). He meant probably Johann Sebastian Bach. "Jesubach" is a new concept formation caused by this thought disorder. Some paralogias seem to be symbolic. Thus one of my Erlangen patients said, "Erlangen is botanical". Why? "Because it has a wreath made of oak and laurel leaves in its coat-of-arms." Another time he pointed to the walls of the living room and stated, "The walls are christianly whitewashed". The pattern on the walls resembled crosses. In this case comparisons became equivalents.

Faulty actions may be the expression of a parapraxia which is related to paralogia: the musically endowed patient with the ambiguous concept of "Bach" poured hot oil into his ears in order to destroy his hearing and to become a famous composer like Beethoven. He also went down one night to the street dressed only in a shirt, because he said everyone was dead and the dead would be buried only in a shirt.

5. In *Incoherent Schizophrenia* in addition to paralogical and paraphasical disturbances there are *incoherences of the stream of thought* associated with a disorder of attention, a slight excitation of thought and phonemes. A patient said, when asked where he was, "Mental hospital, can not be a foundation, as one said . . . house, stones . . . my father . . . family memory, the house where we lived in has also the inscription Karl . . . there I was not ill, Theo is an old warrior again . . . he has suffered a competition in family affairs . . . six, nine, ten families as it were . . . my experiences of childhood has been brought up with fifteen children . . . doctor, no twisting of limbs! . . ."

Quite a few *new word constructions* (family memory) and *paragrammatisms* (my experiences . . . has been brought up) are interspersed in these mental jumps.

In another example paralogias are mingled with the incoherent stream of thought. A patient had to explain the proverb "Der Apfel fällt nicht weit vom Stamm" (The apple does not fall far from the tree). He said, "Das sind Abfälle. Es heisst mit einem Wort unser Stammbaum. Ich sehe mir eine Kiefer an und sehe den Oberkiefer und den Unterkiefer, dann weiss ich, wie der Kiefernstamm aussieht." (These are fallings away. It is called by one word—our family tree. I look at a pine tree and see the "upper pine" (=upper jaw) and the "lower pine" (=lower jaw), then I know what the pine tree-trunk looks like.) The "Kiefer" (pine) as a tree and the "Kiefer" (jaw) as part of the body ("Kiefer" means in German "pine" as well as "jaw") are exchanged, upper jaw and lower jaw appear as father and son. The apple falling off (abfallend) the tree becomes the "Abfall" (transferred meaning: garbage).

Probably the incoherent thought disorder may be referred to a *dysfunction of the diencephalon* in accordance with observations made in brain injuries and cerebro-vascular lesions.

II. PARANOID SCHIZOPHRENIAS

In the paranoid schizophrenias disorders of speech and the above-mentioned impairments of comprehending thought are only slight, whereas a

similar thought disorder concerned with the spheres of *body, personality, social community and cosmic-religious relations* is prominent.

1. A woman with *Progressive Somatopsychosis* complained that her bowels were taken out, her blood burnt, her uterus completely filled, her breasts were as heavy as millstones and her head had disappeared. These strange ideas were supported by bodily sensations. So she misidentified and misinterpreted her somatosensory perceptions and by means of a paralogical disturbance of thought she acquired senseless ideas about the state of her body.
2. A man who fell ill with *Progressive Autopsychosis*, when he was in the army, felt himself mistaken for other men, thought he was given other names, and finally was in doubt of his own identity. Discharged from the army he travelled a long way to his native town in order to find his self. This means he did not recognize himself as the person he was with memories of his childhood, with the experiences of his apprenticeship, his business and his marriage. In a paralogical way his thinking about himself went astray into the ideas of being other people. So he took himself for a corporal, later on for a general, which did not prevent him from doing good work in ladies' tailoring.

A woman with auto- and somatopsychic combined disorders laboured under the delusion that she was a man and shared one head with her husband. She called the former director of the mental hospital her father, said that his predecessor had put his finger into her heart and said it was broken. Many wounded soldiers, "a whole session", hung on her back. Once again these ideas sound symbolical. She put clear and concrete ideas in place of abstractions, which were not available, such as the trivial thoughts of physical and mental unity with her husband, of her security in care of the director, and of her deep affection for the former director. These are paralogical derailments into a lower level of thought with new concept formations which simulate creative performances.

Similar disorders of awareness of self (experiences of self=Eigenerleben) in brain injuries and focal brain lesions point to the cingulate gyrus where afferent impulses from the inner organs and vegetative centres arrive by way of the anterior nucleus of the thalamus. The results of stimulation experiments by Penfield and Rasmussen allow us to postulate the island of Reil as a possible site for the localization of these disturbances.

The *other paranoid schizophrenias* are characterized mainly by symptoms which, from a neurological viewpoint, arise in the *brain stem*. These symptoms are hallucinations (especially phonemes), fantastic ideas, confabulations, experiences of influence and reference. Nevertheless, the cortical phenomena of paralogical disorders also occur.

3. In *Progressive Hallucinosis* a change in the sphere of ideas of social community and finally of the whole of the outside world occurs gradually and this is assisted by numerous auditory hallucinations. The actions of other people are misinterpreted, personal misidentifications occur sporadically.
4. *Phantasiophrenia* presents a lot of fantastic illusions and hallucinations associated with paralogical disturbances of thinking together with absurd new concept-formations which are concerned with all spheres of imagination.

6. Patients with *Progressive Confabulosis* develop delusional formations which are mainly within the sphere of the self and are associated with confabulated experiences. Thought and speech disorders are slight.
7. Only in the final stage of *Progressive Influence Psychosis*, behind the dominating experiences of influence, does a marked deterioration of concepts concerned with the spheres of self and social community occur. Thus one patient attributed the influences in a senseless way to the Jesuits, to an observatory and to the criminal police. *Progressive Inspiration Psychosis* is a variety of influence psychosis in which the influences are experienced as instilled by God or cosmic forces. There is a slight paralogical change of concepts which are concerned equally with the cosmic and religious spheres which led, for instance, in one case to new concept formations in the sense of a vague theological-psychological system. In addition this patient presented remarkable speech disorders with neologisms. Thus he called a garden a "Pflanzenenerziehungsstatte (plants' education centre).
7. The term *Progressive Reference Psychoses* comprises those paranoid psychoses which present with experiences of reference and significance or with over-valued ideas and which show a persecutory delusion at the onset, but later frequently have an expansive delusion. During the further course of the illness fantastical imaginations and sense deceptions sometimes occur. These psychoses are *unsystematic forms of schizophrenia* since the symptomatology spreads extensively over different psychological systems. Only a moderate change of the concepts concerned with self and social community occurs; speech disorders (neologisms) are rare.

In all paranoid forms the emotional bases of the above-mentioned psychological spheres of body and personality, which are represented in the brain stem, are involved. *Progressive Autopsychosis*, *Phantasiophrenia* and *Progressive Confabulosis* are cheerful and expansive; *Progressive Inspiration Psychosis* is ecstatic, *Progressive Hallucinosi*s, *Influence* and *Reference Psychosis* are suspicious or anxious and *Progressive Somatopsychosis* is dysphoric. *Progressive Reference Psychoses* frequently run a course in which opposing emotional states alternate.

Affective changes and fluctuations of mood were observed in brain-injured patients with small shell splinters in the diencephalon, by Hoheisel and Walch (6). They were described by E. Albert (1) in young children with encephalitis and other diencephalic symptoms. Fünfgeld, Jr. (5) and Bäumler (3) investigating Vogt's collection of brains of schizophrenics, discovered loss of nerve cells and atrophic cells (Schwundzellen) in the thalamus, particularly in the medial and anterior nucleus.

III. CATATONIA;

1. The clinical picture of *Drive-poor Catatonia* is dominated by a lack of spontaneity, particularly concerning speech, which neuropathologically is known to be due to frontal lobe lesions. A decrease of the stock of words results in monotony of verbal expression. Agrammatism of various degrees often occurs. Thus the symptom complex also includes the motor-aphasic syndrome. There is also an impairment of active and creative thought, i.e. an alogical thought disorder with simple failure and imperfect thought performances, which I have also observed in injuries and diseases of the frontal brain.

A patient described the picture of "blind man's buff" (Blindekuh) in the following way, "I see it, I also know what it means, the crying shame." He explained the picture of "the broken window pane" as follows, "These are blackguards, good-for-nothings, the pane broken, monster." Another patient was asked to differentiate between child and dwarf: "Grosser Unterschied . . . durch Bestehen, durch Herkunft . . . es ist im allgemeinen, wo eben schon besteht . . . durch Arbeit. Der Zwerg versteht wie anders das Kind, wo gleich gross mit ihm dasteht." (Big difference . . . by existence, by origin . . . it is in general where there already exists . . . by work. The dwarf understands as otherwise the child, who exists, as tall as he.) The monotony should also be noted.

In all the other varieties of *catatonia psychomotor* signs due to the disorders of the brain stem are predominant.

Akinetic and Parakinetic Catatonias are of an antagonistic nature and characterized by psychokinetic playful impulses (spielerische Regungen) arising from the brain stem.

2. The *akinesia*, i.e. the lack of impulses, is associated with a restriction of movement, dyskinesia, waxy flexibility, automatic co-operation and *Gegenhalten* (automatic resistance). Similar states occur in focal lesions of the pallidum and thalamus. Hopf (7) has found atrophic cells (Schwundzellen) and loss of cells in the pallidum of catatonics which could not be observed in the brains of other schizophrenics of Vogt's collection. I have had the opportunity to convince myself of this fact.
3. The *parakinetic increase of impulsive activity* results in distorted and eccentric movements which remind one of *chorèa*, athetosis and torsion dystonia. Parakinesias and other hyperkinesias due to focal brain lesions are localized in the striatum, especially in the caudatum and the thalamus. They were also observed due to small shell splinters in the diencephalon during World War II (Zülch (25) and Cl. Faust).

Negativistic and Proskinetic, Stereotyped and Iterative Catatonia can be considered as two opposed pairs which are characterized respectively by the strivings of negation and affirmation, of stereotypy and repetition. These disorders can be localized in the brain stem.

4. The "*forced antagonistic innervation*" observed by E. Beck (2) in a post-encephalitic state where other symptoms also indicated a brain stem lesion is related to negativism.
5. The affirmatory tendency of the *proskinetic catatonics* (as described by Leonhard) is in accordance with their turning towards the examiner (*Zuwendung*), with their meeting him half way (*Entgegenkommen*), and their readiness to imitate. The patients seize everything they see and everything which touches them, in a short-circuiting manner. They show tapping, plucking and picking movements and talk only in a whispering voice. They yield to passive movements without remaining in given postures and offer an automatic obedience. Echo responses and *Vorbeireden* (talking past the point) also characterize Leonhard's "Speech-prompt Catatonia".
6. In *Stereotyped Catatonia* verbal utterances and stereotyped movements occur which differ from the uniformity of drive-poor catatonia because of their mannerisms and a certain restlessness.

The *Iterative Catatonia* differs from the other catatonias by a greater variation in its symptoms of restlessness and other features, as well as by its course with remissions and the final picture of a milder stage of defect. Therefore Iterative Catatonia (or "Periodic Catatonia" as designated by Leonhard) belongs to the *unsystematic* and *extensive* forms of schizophrenia. Stereotypies and iterations similarly occur in focal lesions of the brain. They are localized in the striatum, particularly in the caudatum. Together with my co-workers Herz and Pittrich (9) I was able to take motion pictures of all catatonic symptoms and clinical pictures.

IV. HEBEPHRENIAS

. *Apathetic Hebephrenia* is characterized by a simple affective devastation and an ethical flattening, increasing as the illness proceeds, and interrupted only by brief changes of mood and states of excitement. Drive (Antrieb) decreases to the same degree, and thought tests reveal an alogic defect.

An orthodox Jewish patient no longer bothered about her religious duties, neglected her clothes and became voracious. She smeared when eating, licked the other patients' plates, rummaged for edible things in the garbage and went begging from passers-by without any shame. Sometimes she wandered about naked or lay apathetically and inertly on the floor.

. *Silly Hebephrenia* and (3) *Depressive Hebephrenia* present, beside a less marked affective and ethical flattening, affective changes of a silly cheerfulness or of a discontented and hypochondriacal depression associated with eccentric habits. These changes of mood gradually fade. Affective blunting, impoverishment of drive, and alogic thought disorder remain.

Two examples: "What is the difference between chest and basket?" Patient's answer: "I know what kind of a difference there is." "Difference between staircase and ladder?" Answer: "This is undoubtedly a difference."

. Leonhard's *Autistic Hebephrenia* differs from the other forms by its constant autism associated with suspiciousness, persecutory delusions, and frequent sense deceptions which decrease later on.

Seen from a neuropathological point of view, the ethical regression of the hebephrenics is comparable with the changes of character occurring in injuries and focal lesions of the *orbital brain*. The cheerful and depressive swings of mood in Silly and Depressive Hebephrenia resemble the phase-like changes of mood in cases with shell splinters in the *diencephalon* as reported by Hoheisel and Walch (6). Affective blunting is also due to disorders of these structures.

In considering the multiplicity of schizophrenic symptoms and syndromes with their neurobiological connections between the cerebral cortex and the brain stem, I am unable to see a common factor associated with or comprising all these symptoms. I do not find any hint of a consistent pathophysiological *basic disorder* which Berze believed to have found as a "Hypotonia of consciousness" based on a primary insufficiency of psychic activity. Recently Wyrsh (24) has mentioned a "*schizophrenic basic mood*", i.e. a peculiar mood and a special state of consciousness. But these are phenomena too vague to be useful, and besides they only occur in cases of recent illness. This also applies to the *powering of the "I" quality* of perception, feeling, thinking and willing. Moreover, such depersonalization is also seen in certain psychoses of alienation which are related to endogenous depressions. Wyrsh's specific symptoms of

autism and splitting of personality not only do not occur even in all schizophrenics but also occur in non-schizophrenics. Carl Schneider (21) has assumed three different schizophrenic basic disorders which, on the whole, are supposed to be associated with each other. They are considered to release three symptom complexes, viz. "Gedankenentzug" (thought withdrawal), "Sprunghaftigkeit" (desultoriness), and "Faseln" (drivelling). But these symptom complexes do not cover the diversity of schizophrenic symptoms and the attempt to deduce the remaining symptoms from a coincidence of more than one complex appears to me to be artificial.

Secondary symptoms which arise from a partially intact mental life, as a response to the *primary* morbid symptoms, must be omitted here. According to their nature they cannot possess any cerebro-pathological correlations. These secondary symptoms are the "Erlebnisformen" (forms of experience) of mental illness described some time ago by Jaspers and Mayer-Gross and elaborated recently and enlarged as the "*Daseinsformen*" (forms of existence) by L. Binswanger and others.

Although no general fundamental schizophrenic disorder has been discovered until now, schizophrenics participate in their *own peculiar way* in all symptoms and clinical pictures which occur in psychoses. In grouping the various psychotic states according to their similarity or difference with states of a healthy mental life the schizophrenias make up almost half the group of *heteronomous syndromes* which are foreign to the normal psyche. These are e.g. the states of thought- and speech-deterioration with paralogic-paraphasic lapses, the states of ethical flattening and affective blunting. They are *axis syndromes* (in the sense of Hoche) of the schizophrenic illnesses. On the other hand, the states of disordered consciousness, waking, memory, orientation and recollection (alteration of consciousness, sleepiness, twilight state, delirium and amnestic syndrome) are not schizophrenic. They do not belong to the schizophrenic psychoses which we assume to be of a "fine-organic" nature, but they belong rather to the gross-organic traumatic, circulatory, senile, inflammatory epileptic and symptomatic (toxic-infective) psychoses.

The *intermediate syndromes* which are not quite so remote from a normal inner life belong for the most part to the schizophrenic states. These syndromes are the states of striving, especially negativism and autism, certain states of psychokinetic impulses (Regungen), i.e. akinesia, parakinesia and hyperkinesia, and hallucinosis, confabulosis, fantastic excitation and the states of influence, reference and significance. Among these symptoms there are some that occur more frequently than others (for instance auditory and somatosensory hallucinations, experiences of influence, reference and significance). But in the intermediate syndromes there participate also—although they have other centres of gravity—the symptomatic as well as certain phasic psychoses which are closely related to manic-depressive illnesses.

The *homonymous syndromes*, particularly the affective ones, which resemble the states of a healthy inner life do not occur as pure forms in schizophrenia, but they accompany and colour schizophrenic syndromes. This group of homonymous syndromes is mainly made up by the manic-depressive psychoses and phasic psychoses closely related to them.

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PSYCHOLOGICAL MEASURES AS USED TO PREDICT PSYCHIATRIC IMPROVEMENT AND TO ASSESS BEHAVIOURAL CHANGES FOLLOWING PREFRONTAL LOBOTOMY*

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I. INTRODUCTION

THE advent of the various tranquillizing drugs during the past few years and their increasing use in mental hospitals have had the effect of drastically decreasing the number of lobotomies performed. At our hospital, e.g., the last lobotomy was performed in November, 1954; previous to that time 131 such operations had been done in seven years. To all intents and purposes lobotomy is a therapeutic procedure no longer used for psychiatric purposes. This may change, of course—it may be decided that for certain patients a lobotomy is still the treatment of choice. Or, it may be that in the years to come lobotomy will be of interest chiefly to medical historians.

In any event, it seems desirable that we assess, as well as we can, the effects of the operation. Such information—quite aside from indicating possible therapeutic uses of lobotomy—may prove of theoretical value in furthering our understanding of brain functioning, and of heuristic value in our evaluations of other therapies.

The investigation to be reported here was carried out at the Palo Alto Veterans Administration Hospital from 1951 to 1955. It consisted, in the main, of the administration of certain psychological procedures to operated patients, both before and at intervals following operations; of the comparison of the obtained measures to certain available criterion data; and of the evaluation of changes in these measures over time.

* From the Veterans Administration Hospital, Palo Alto. The test battery used in this study was selected and/or developed by the senior author; the data were tabulated and analysed by the junior author; and both authors are responsible for this report. A number of other persons also participated extensively in this study. The patients were examined primarily by psychology trainees under the supervision of Dr. Richard C. Hamister. Mary Ann Swanson contributed greatly in the scoring and collection of data. The authors are particularly indebted to Dr. Kenneth P. Jones, who with the assistance of a large number of ward physicians, collected the criterion data. These data were collected for another study (7) but were generously made available to us. The physicians who assisted Dr. Jones were: Drs. G. Altbach, Wallace G. Beckman, Franklin C. Cassidy, Abram Dansky, Harry Elkins, Emerson Hiler, Genevieve Knupfer, Alan J. Kringel, William R. Meadows, Harold Mikkelsen, L. Mitchell, Robert S. Mowry, Judith Musladin, R. G. St. Pierre, David F. Shupp, John O. Smith, Leo M. Traub, and John A. Withrow. Dr. Robert L. McFarland had much to do with setting up the criterion rating system. Dr. Alexander Simon made a number of helpful suggestions during the planning phase of the study. Drs. Glenn Brackbill, John Daily, Richard Hamister, and S. D. Schultz generously acted as judges of Rorschach protocols.

II. GENERAL PLAN OF THE STUDY

1. *The Lobotomy Programme at Palo Alto*

The lobotomy programme was inaugurated here in June, 1947. The last operation was performed in November, 1954. During this time 131 patients were operated—all but four having bilateral operations. Six patients died before follow-up criterion data had been collected. If these deaths are eliminated from consideration there remain 125 patients. Criterion data were gathered for this sample of 125 in November, 1955. The effective closing date of this study is thus November, 1955, which is one year after the date of the last operation.

At this hospital lobotomy was considered a treatment of last resort and was used only with patients who were extremely ill, and who had not improved under all other available forms of therapeutic intervention. The hospital was quite conservative in ordering the operation and routinely insisted that all other therapies be tried and found ineffective before a lobotomy was undertaken. Consequently, the operated patients comprised a sample of extremely ill and chronic subjects, such that almost any degree of overall improvement, had the operation not been performed, would have been unlikely.

2. *The Criterion of Improvement*

In order to evaluate the effectiveness of lobotomy it was necessary to have a measure of improvement after the operation. The improvement criterion used at this hospital was adapted from that used in the Columbia-Greystone (12) study. A modification of this scale first was used at this hospital in a study by Becker and McFarland (1) in their development of a lobotomy prognosis scale. In a report made in 1956, Jones (7), reporting on general lobotomy follow-up data, used a scale almost exactly like that used in the Columbia-Greystone study. As used by Jones the scale consisted of 5 steps, as follows:

- 0=Minimal or no improvement, patient on disturbed ward.
- 1=Patient on moderately disturbed ward, no ground privileges.
- 2=Patient has ground privileges.
- 3=Patient at home, under supervision.
- 4=Patient at home and working or capable of working.

Since the great majority of patients given lobotomies at this hospital were from disturbed wards*, the placement of patients on the above scale at some period after the operation would give a good approximation of the degree of improvement attained by those patients. Dr. Kenneth P. Jones, in November, 1955, obtained data to rate each of the 125 lobotomized patients on the above criterion. These data were furnished by the various ward physicians who had lobotomized patients under their care. On the basis of the reports Jones, who was the psychiatrist in charge of the ward to which most post-leucotomy patients were assigned, prepared a report (7) of the clinical course of the lobotomized patients.

Of the 125 patients, 22 obtained ratings of 0; 43 ratings of 1; 36 ratings of 2; 2 ratings of 3; and 12 ratings of 4. These distributions are presented graphically in Figure 1. It is to be noted that all of the 125 patients were rated at the same time—November, 1955. For some patients this was seven or eight years after the operation, for one patient as little as one year after operation.

* The number of patients from other wards was so small as not to merit separate consideration.

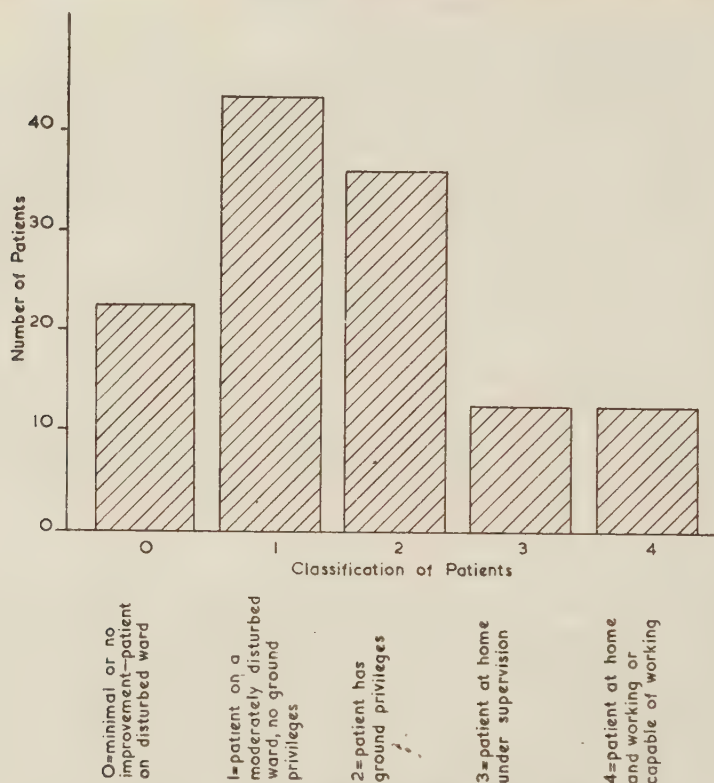


FIG. 1.—Classification of lobotomized patients as of November, 1955*.

* All operated patients were classified on the above scale November, 1955, regardless of when they received lobotomies. At least one year had elapsed between operation and rating for all patients.

It would have been preferable, for analysis and interpretative purposes, if the ratings had been obtained the same number of months or years after operation for each patient. It was not possible to do this, however, the fact that the criterion ratings for the different patients are based on different post-operative intervals, while unfortunate from the standpoint of experimental design, is probably not overly significant*, since it is generally believed that such changes as may follow a lobotomy occur predominantly within the first post-operative year.

These ratings, as obtained by Jones (7) in November, 1955, provided the basic criterion data for the study to be described in this paper.

3. The Lobotomy Psychology Testing Programme

The research lobotomy testing programme was begun in May, 1951, and terminated in April, 1955. The general plan of the programme was to administer, to each patient selected for lobotomy by the Hospital Lobotomy Committee, certain prescribed tests. These tests were given before the operation, 10 days following the operation, and at intervals of 5 weeks, 3 months, 6 months, and

* The correlation coefficient between the criterion ratings and the time since operation is equal to .10, which is not significantly different from zero. This indicates that there is no significant over-all change in ratings after the first year following lobotomy.

year after the operation. The prescribed test battery was somewhat different for each of the periods. Table I presents the names of the tests involved, and the

TABLE I
*Schedule for Psychological Testing of Lobotomy Patients**

Tests	Time					
	Pre-operative	10th Day	5th Week	3rd Month	6th Month	12th Month
Rorschach	×					×
Draw-a-Person	×		×			×
Modified Porteus Maze	×			×		
Gender-Gestalt Cards 4 and 7	×	×		×		×
Concept Evaluation Technique	×	×		×	×	×
Colour Naming	×	×	×	×	×	×
Digit Symbol	×	×	×	×	×	×
Object Memory	×	×		×	×	×
Wechsler-Bellevue Vocabulary				×		
Sentence Completion	×		×		×	×
Motor Inhibition	×	×	×		×	×

* These tests are described in III 2 below. As already noted it was often impossible actually to obtain test data according to the above schedule. The schedule is best interpreted, therefore, as indicative of when attempts were made to obtain certain test data.

intervals at which they were to be given. During the period of the study 73 cases were assigned for research psychological testing. Testing was done primarily by psychology trainees and to the extent possible each patient was tested throughout by the same examiner. Of the 73 patients assigned for psychological testing, many were unable to take certain of the tests or, for various administrative reasons such as illness, trial visits and the like, were not tested at a given scheduled period. Thirty-four patients, e.g., were not given any of the pre-operative tests. The number of patients completing a given test at a given period ranged from 23 to 56.

The purposes of the lobotomy testing programme were to obtain additional information on the following two questions:

1. How useful are psychological tests in predicting which patients will benefit from lobotomy? and
2. What are the changes in mental functioning over time following lobotomy?

Obviously both of these questions are of such size that we could not hope to answer them definitively. Rather, our hope was to make a significant addition to a literature already rather voluminous (5, 6, 8, 12, 14, 16, 17, 18, 19).

In choosing the tests to be included in the battery we were guided by several considerations: (1) the procedures should be relatively brief and should be easily administered—since many different examiners would be involved; (2) as much as possible the procedures should be amenable to the most depressed of patients, since a great many of the patients to be operated were, in terms of standard test batteries, “untestable”; and (3) the procedures should have some relevance—either in terms of previous studies or on theoretical grounds—to the rationale of lobotomy.

Since we could include only a limited number of tests, no attempt was made to be comprehensive in sampling psychological functions. We were not attempting to develop a “better” battery than other investigators and did not select tests to comprise the best possible battery. Some of the tests were chosen because they are commonly used psychological instruments (e.g. Rorschach); some were included because there is evidence that they are related to the effects

of lobotomy (e.g. Motor Inhibition (3, 16)); some were included because it was believed that almost any co-operative patient, no matter how regressed, could take them (e.g. Colour Naming); and one (Concept Evaluation Technique, or CET) was included because of an hypothesis concerning its relation to the effects of lobotomy. In addition to the actual tests taken each patient was asked to help plan the order of the tests: this was to obtain data with which to evaluate the common hypothesis that lobotomy has a detrimental effect on the patient's foresight and planning ability. Each patient was also asked to estimate how long he had been on his ward, how long in the hospital, how much time the testing required, and the number of tests taken.

The nature of the tests used, and the constitution of the samples studied with them will be described in Part III.

4. *The Behavioural Rating Scale*

In order to obtain data concerning ward behaviour of the patients studied, the Hospital Adjustment Scale (4, 9) was used. Unfortunately the use of this scale did not commence until some time after the beginning of the study and, further, it was not possible to obtain periodic HAS ratings on all Ss even after use of the Scale was undertaken. Consequently, an insufficient number of HAS scores were obtained for these to be of use as an additional criterion in evaluating the predictive adequacy of the pre-operative psychological tests.

However, by comparing the HAS scores with the criterion of improvement ratings discussed in II 2 above it was possible to obtain information concerning the validity of the HAS, and this information is presented in V below. Further, it was possible to use HAS scores as a means of evaluating changes after lobotomy, and these findings are reported in IV 2 below.

III. PREDICTIVE VALIDITY OF THE PSYCHOLOGICAL TESTS

1. *Subjects*

As noted earlier, a total of 73 patients, including 69 males and 4 females, were seen one or more times for psychological testing. Because of the small number of females separate analyses were not carried out for each sex. Of the 73 patients, 14 had a criterion rating of 0; 23 of 1; 22 of 2; 8 of 3; and 6 of 4. Of the original group of 125 patients classified in the Jones study, all but two were diagnosed as schizophrenics. The ages of the 125 patients at the time of operation ranged from 20 to over 60 with the median age at 33*.

As already noted, the patients were so ill that it was often impossible to obtain adequate test data. Consequently, the number of patients on whom test data were available differed appreciably from test to test, and from testing period to testing period.

2. *The Predictive Validity of the Tests Against the Criterion of Improvement Ratings*

Due to the great differences in the scoring systems used for the various tests it was not possible to use one measure of comparison for all tests. Where the test scores are continuous variables which could be considered as coming

* These data were not tabulated separately for the 73 patients used in the psychological testing programme. It was assumed that this latter sample, selected only on the basis of date of operation, would have approximately the same characteristics as the 125 patient sample, i.e. homogeneity as to diagnostic classification and heterogeneity as to age. The age distributions would vary somewhat from test to test, and sufficient patients in each age group would not be available for any one test to make age a variable worth including in the analysis.

from approximately normally distributed populations, the Pearson product-moment correlation coefficient was calculated. The results for these tests are presented in Table II. The method of comparisons varied for the other tests.

A few brief comments will be made about the findings for each test procedure.

TABLE II

Correlations Between Certain Pre-operative Test Scores and Criterion Ratings

	Test						N	r
Bender (Cards 4 and 7)	..	..	..	..	..	..	39	-.11
Concept Evaluation Technique:								
J score	..	..	..	..	..	..	28	-.42*
V score	..	..	..	..	..	..	23	-.24
E score	..	..	..	..	..	..	23	-.14
Digit Symbol	..	..	..	..	..	..	37	.12
Object Memory:								
Immediate	..	..	..	..	..	..	31	.06
Delayed	..	..	..	..	..	..	28	.19
Porteus Maze (modified scoring)	..	..	..	..	..	..	33	.23

* Significantly different from zero at the .013 level (one-tailed test). None of the other coefficients reached statistical significance.

Bender-Gestalt. Cards 4 and 7 of this test were administered, and were scored by the Pascal-Suttell (13) scoring system. The correlation of the sum of these two cards with the criterion rating was not significantly different from zero.

Concept Evaluation Technique (10). The three scores obtained on this test, J, V, and E, were each correlated separately with the criterion. The only correlation of any significance is that for J; this is significant at the .025 level for a two-tail test. Inasmuch as it was predicted in advance that this relationship should be negative, a one-tail test is not inappropriate—yielding an .013 level of significance. The negative correlation indicates that a high J score, pre-operative, is contra-indicative for improvement from lobotomy. The theoretical interpretation of this result will be further discussed in III 4.

Colour Naming. The Colour Naming test given was that presented in Wells and Ruesch's Handbook (21). It was scored for both time and errors. The number of errors was mostly zero or very small, and hence not applicable to analysis. Since the distribution of time scores was highly skewed, a correlation coefficient was not calculated. The medians for each criterion group were computed: they showed no apparent trend.

Digit Symbol. This test was the digit symbol test of the Wechsler-Bellevue (20), either Form I or Form II. In most instances Form I was used for pre-operative testing. Weighted scores were correlated with criterion ratings, and the correlation was insignificantly different from zero.

Draw-a-Person. Most patients were asked to make only one drawing; this was usually of a man. For patients who had drawn both a man and a woman, only the drawing of the man was scored. The drawings were rated as "good", "fair", or "poor" by one of the authors (M.W.). "Poor" meant that the drawing was primitive or bizarre. An appropriate tetrachoric correlation coefficient was computed by grouping together the ratings of "good" and "fair", and by

grouping criterion classifications 0 and 1 against 2, 3, and 4. The obtained coefficient, $\cdot 19$, is not significantly different from zero.

Motor Inhibition. This test was adapted from the Downey Temperament Scale (3), and had previously been used in lobotomy research (16). The patient was asked to write "United States of America" as slowly as possible but with the pencil always moving. He was told that some people could take as long as one-half hour to do this. The length of time taken by the patient was recorded. The distribution of these times was highly skewed, hence, only the medians for each classification criterion were computed. These failed to show any apparent trend.

Object Memory. Close to the beginning of the testing sessions the S was asked to identify the pictures of 10 objects (21, page 155) and then was asked to recall them immediately after the identification. Near the end of the testing session he was again asked to recall the objects from memory. The number of objects correctly recalled from these two trials were both correlated with the criterion ratings. Neither correlation was significantly different from zero.

Porteus Mazes (15) (Modified Scoring). The usual Porteus scoring method was not used. Instead each S was given a score corresponding to the highest age level at which he successfully completed a maze on any of the trials allowed. This variable did not correlate significantly with the criterion ratings.

Sentence Completion. A special sentence completion test was developed for this study. Five scores were obtained for this test: (a) the number of sentences attempted; (b) the percentage of these which were grammatically correct; (c) the percentage which showed perseverances in language or thought expressed; (d) the number out of a selected group of five sentences which showed a positive affect; and (e) the number out of these five which showed negative affect. Since there were no apparent trends when these data were compared with criterion data, detailed analyses were not performed.

Vocabulary (Wechsler-Bellevue). This test was not administered before the operation.

Planning. The Ss were rated as: (a) unwilling to help plan the order of testing; (b) willing but unable to help plan the order of testing; or (c) helped plan the order of testing. These data showed no trends when compared with criterion data; most patients in all criterion groups were unwilling to attempt planning the tests.

Estimates. Patients were asked to estimate: (a) the times required for testing, the time they had been on their ward, and in the hospital; and (b) the numbers of tests given. When these estimates, expressed as percentages of actual times or numbers, were compared with criterion ratings no trends were apparent, and no detailed analyses were performed.

Testability. It was felt that the testability or untestability of the patients before operation might itself be related to post-operative improvement. Inspection showed that approximately 50 per cent. of *all* criterion classifications were untestable before the operation, however; hence this dichotimization had no predictive value.

Rorschach. The Rorschach data were analysed in two ways, as follows:

- (a) The total number of responses given and the breakdown of this number by determinants was considered. These results were converted to T-scores (2) for analysis. Figure 2 gives the psychograms of the mean scores for each classification group. The FM scores seemed to have a fairly widespread scatter; hence, a one-way analysis of variance was performed to test the

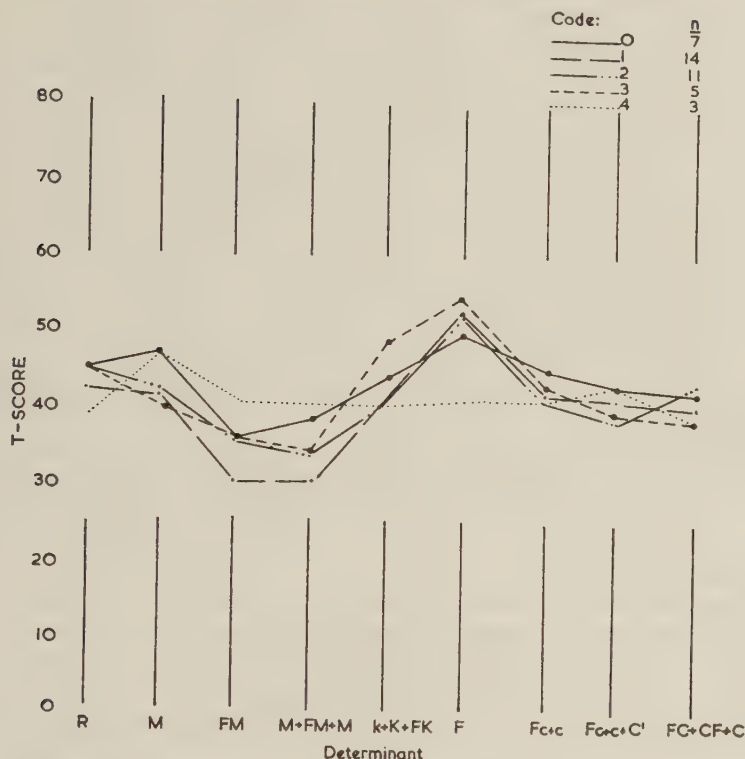


FIG. 2.—Pre-operative Rorschach psychograms of mean t-scores by classification groups.

differences among the means. The results were not significant, and accordingly no further analyses of scores were undertaken.

- (b) Four experienced clinical psychologists, all of whom were familiar with both Rorschach procedures and lobotomy follow-ups, were given the available Rorschachs ($N=38$) for judgment. On the basis of these protocols they predicted the criterion rating each of the 38 patients would receive. These predictions were correlated with the actual ratings; none of the correlations approached significance. They ranged from $-.01$ to $.15$.

3. The Predictive Validity of the Tests Against the Criterion of Behavioural Ratings

As mentioned before, the Hospital Adjustment Scale also was considered for use as a criterion of improvement. However, there were not a sufficient number of ratings made at any one period, either around a given date or a given time after operation, for this to be possible.

4. Discussion of Findings Concerning the Predictive Utility of the Tests

The findings of this study, as so far reported, are, with one exception to be discussed presently, negative. The utility of the instruments used to predict whether or not, and how much patients will improve after lobotomy is so little as to provide no justification for the inclusion of the instruments in any battery of tests designed to help select patients for operation. There are, of course, extenuating circumstances. For one thing, *the population studied was very*

homogeneous—all of the patients were very seriously ill and *all had passed through several screenings prior to being tested pre-operatively*. The point here is this: that in effect “the cards were stacked” against the tests from the beginning: the tests used might well have proved valid if the sample had been more heterogeneous—they might well have proved useful in screening patients to be considered for lobotomy. But the practical conclusion seems to be, nevertheless, that *those tests used in this study*, had they been used as selective criteria for determining which of the patients considered in this study should have been operated, would not have added materially to the adequacy of such selections.

The one exception to this generality is the J score of the CET (Rorschach Concept Evaluation Technique). It is interesting to note that this is the one test score in the whole battery for which a specific hypothesis was formulated in advance of the testing. This hypothesis was that J should correlate negatively with improvement after lobotomy. As noted in Table II this hypothesis was confirmed ($r = -.42$).

The CET (10) is a procedure in which the S is successively shown 50 areas on the Rorschach blots and asked, for each one, if it could be some specified object. Thus, item number one involves the presentation of blot 1 with the question “Could this be a bat?” The S simply answers Yes or No. The number of Yes answers he gives for the entire 50 presentations is counted, and this value is translated into a T-score. This T-score is referred to as J. The actual finding, therefore, was that those patients with initial low J-scores have a better chance of improving after lobotomy than those patients with initial high J-scores.

What is the meaning of this trend? And why was such an hypothesis formulated in the first place?

The J-score is assumed to measure the degree to which a S's standards of evaluation, or conceptualization, are strict and demanding—at the one extreme, or loose and non-rigorous—at the other extreme. To quote from a previous publication (10, page 66): . . . “The hypotheses for a low J-score would be that this individual tends to maintain, in his thinking, strict standards of evaluation, to have highly channelized thought patterns which would tend to revolve endlessly about a few subjects. He would tend to be ruminative, to take things seriously, to carefully consider all sides in making a decision. A high J-score, on the other hand, might suggest ramblings and tangential thought patterns, a tendency not to be ruminative or to take things seriously.”

If this is what J measures, then what is the predicted effect of organic intrusions on these functions? Previous work and experience has suggested that patients with cerebral organic pathology tend to have high J-scores. It was therefore a rather straightforward expectation to suppose that the effect of lobotomy—which is a physiological intrusion—would tend to be to effect a raising of the J-score. This would mean that patients whose illness was manifested in a too-low J-score should tend to benefit from the operation, whereas patients with a too-high J-score should tend not to benefit from the operation. These effects would yield a negative correlation between J-scores and improvement.

There is one other interesting point to be made here, of a rather speculative kind. The above evidence would indicate that a patient's standards of conceptualization tend to become looser, less strict, after lobotomy. Now, there is also evidence—not from this study, but from the Columbia-Greystone study (12, p. 305, 311)—that following lobotomy there is often a marked decrease in level of anxiety. These two tendencies may be functionally related.

One of the authors of this report (P.M.R.) has proposed a theory (11) in which anxiety is equated with magnitude of unassimilated material. To bring about a reduction in level of anxiety an anxious person would have somehow to assimilate a sizeable portion of this material. Since assimilation is basically a process of conceptualization it follows that assimilation would be easier if one's standards of conceptualization were made less rigorous. Hence lobotomy—which appears to bring about a lessening of the standards of conceptualization (according to the evidence of this study)—could be expected to tend to effect a lowering in anxiety level (as indicated by the Columbia-Greystone data).

The finding that J-scores are negatively related to improvement after lobotomy can also be reconciled with the views of Jenkins (6, p. 87) on the nature of schizophrenia and lobotomy. Jenkins conceptualizes anxiety as being due to a morbid degree of resonance between the pre-frontal lobes and the diencephalon. Such a circuit of self-sustained neural activity would possibly cause a patient to become concretistic in his conceptualizing. If, then, the operation reduces the tendency toward "morbid resonance of neural circuits", as Jenkins postulates, it might also result in a lessening of the overly-rigorous conceptual standards.

IV. PSYCHOLOGICAL AND BEHAVIOURAL CHANGES FOLLOWING LOBOTOMY

1. *Test Changes Over Time*

As indicated in Table I, the general plan of the study called for giving the same, or equivalent, test procedures to the same Ss at different pre-determined times following operation. It would seem that the resulting data should be particularly useful in assaying test changes following lobotomy. Such analysis should be especially pertinent to the question of what mental functions and capacities are improved or hindered by lobotomy and might possibly bear upon the greater question of which psychological functions are subserved by the frontal areas.

Actually, however—and unfortunately, the data available were far from ideal for analyses of this kind. Due to the facts that many patients, on any given test, were often untestable—or for various reasons of practicability were not tested, it happened that the number of cases on whom successive testings on the same tests were available was quite small. However, for most of the tests the number of patients tested at each scheduled testing period was sufficient to indicate trends. The point here is that while the Ns of Ss tested at each scheduled period were, for the most part, satisfactory, these Ns were not comprised of the same patients throughout. Consequently, the trend analysis data have to be interpreted as suggestive rather than as demonstrative. With this point in mind we may consider the general findings, which are presented graphically in Figure 3. For descriptions of the test procedure used see III 2.

Bender-Gestalt. As indicated in Figure 3, Bender scores (based on cards 4 and 7 only) show an increase from pre-operative testing to the testing ten days after operation, and then a general decline to the 12th month testing. Since a higher score denotes poorer performance, it is evident that performance was somewhat poorer immediately after surgery, and then gradually improved. It is not possible to evaluate the extent to which this change is due to practice.

Statistical Tests. Before going further several comments should be made about the place of statistical tests in evaluating changes over time. The Bender results, as summarized above, were not evaluated statistically in order to determine whether or not the changes over time (Fig. 3) were reasonably attributable

to chance. Similarly, such statistical tests were not made for any of the test changes over time. The reason for this is that—as noted earlier—the means obtained at each testing are based upon different but overlapping samples. This meant that valid significance values could not be attached to any statistic associated with the evaluation of trends, and, consequently, the results of statistical analyses would have been only suggestive. They would have given no more information than that obtained from an examination of the data in graphical form. If trend analysis had been restricted to those cases on whom successive testings were done, the number of cases would have been too small to justify much concern. Hence, it was deemed best to present the data for all cases available even though the trends must be interpreted as only suggestive.

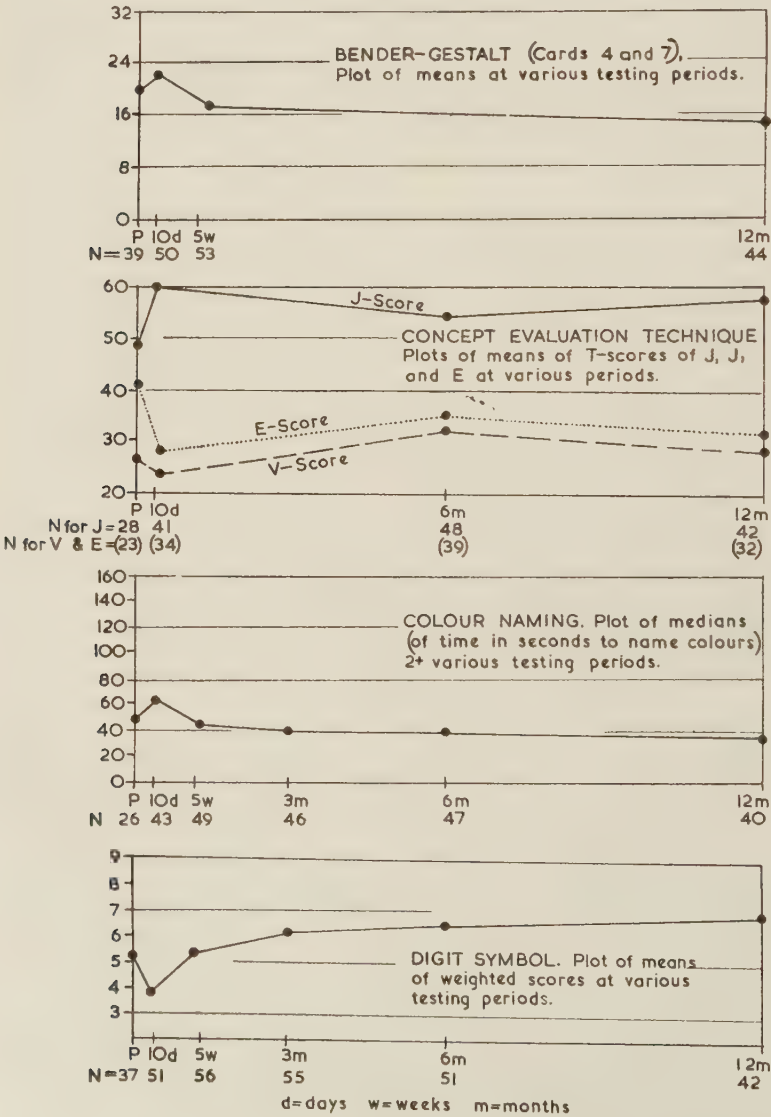


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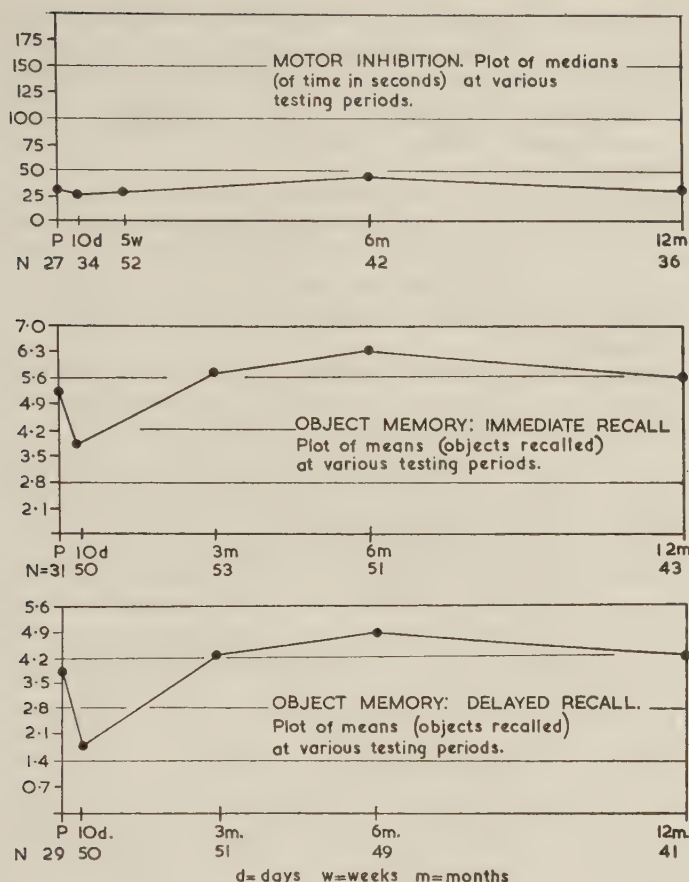


FIG. 3.—Plots of test scores against time after lobotomy*.

* Ordinates refer to test scores, abscissas to time. The extent of variability can't be evaluated in terms of the range—in most instances the ordinates represent about one-half the range. The symbol P refers to Pre-operative scores.

The data are plotted on roughly comparable scales: for each test the range of values presented is about one-half the average range of test scores obtained.

Concept Evaluation Technique. As indicated in Figure 3 the J-score rises immediately after the operation and then tends to level off. The initial increase was more marked for patients who later obtained higher criterion ratings. The V-score showed an immediate decrease and then apparently an increase followed by a levelling off. The E-score showed a marked initial decline followed by a slow rise. The J-score trend is to be expected on the basis of previously discussed hypotheses; the V-score trend probably reflects an initial confusion followed by a minimal increase in degree of contact with reality; and the E-score trend can be interpreted as an initial loss of rigidity, followed by a trend toward increasing rigidity—which, however, never reaches the pre-operative level.

Colour Naming. Figure 3 presents the trend—in medians, which seemed more appropriate in this instance than means—for time required to name the colours. There is little change over the successive testings. Since the number of errors was heavily skewed toward zero, these data were not appropriate for analysis.

Digit Symbol. Here we note a drop immediately following operation, and then a gradual increase which appears to have levelled off by the end of one year. From inspection it appears that changes on this test are among the most dramatic found in this study. A suggestive implication is that the test improvement is due to an increased ability to concentrate, and, perhaps, an improved motor co-ordination.

Draw-a-Person. This test was given three times—pre-operatively, after five weeks, and after one year. The mean ratings assigned to the protocols are almost exactly the same for the three periods, and are not presented in Figure 3.

Motor Inhibition. Figure 3 shows the trend over time for this test, as plotted in medians, which in this instance were more appropriate than means. There is practically no change.

Object Memory. There were two parts to this test: the recall of objects *immediately* after seeing them, and the recall of objects after a *delay* corresponding to the rest of the testing session. As noted in Figure 3, both parts have similar curves. If one overlooks the decrement immediately following operation, then the curves are indicative of a general improvement which reaches a maximum at about 6 months, and then tends to decline.

No other test trends are included in Figure 3. In the case of the Porteus Mazes data were not available beyond the third month, and in the case of Sentence Completion none of the scores, for various reasons, were appropriate for examination of trends. There were no clearly discernible trends in terms of patients' ability to plan the tests, or in the accuracy of their estimates of time required for testings, and the like.

2. Behavioural Rating Changes Over Time

The Hospital Adjustment Scale (4, 9) was used—to the extent that clinical duties of ward staffs permitted—in order to evaluate actual behavioural changes shown by post-lobotomy patients. There were about 100 different patients rated at one time or another on the HAS, but, for various practical reasons, it was impossible to hold to a very precise schedule in terms of when ratings were obtained. Consequently, the groups of patients rated at any one interval period after surgery are to some extent different from the groups rated at other interval periods, and the number of cases on whom ratings were available also varies greatly from one period to another. Figure 4 presents the means for the various yearly intervals after lobotomy of the HAS total ratings. Statistical tests for the significance of trends revealed in these curves were not carried out. Such tests would have been inappropriate because of the facts just noted: that the patients involved, as well as the sample sizes, varied from interval to interval.

In the interpretation of these curves there probably is a certain degree of bias as the intervals get further from the date of operation—i.e. the later values may be somewhat too low since they obviously were based on patients still in the hospital, and did not include patients who had improved enough to be discharged. This number was small, however, and any such bias is minimal. It is to be noted that patients were included in the HAS ratings who had been operated several years before the psychology testing programme was undertaken. This made it possible to obtain ratings for periods up to eight years following surgery.

It is further to be noted that only one HAS score—the total score—is reported. Actually, the HAS includes also three sub-scales—concerning communication and interpersonal relations; care of self and social responsibility;

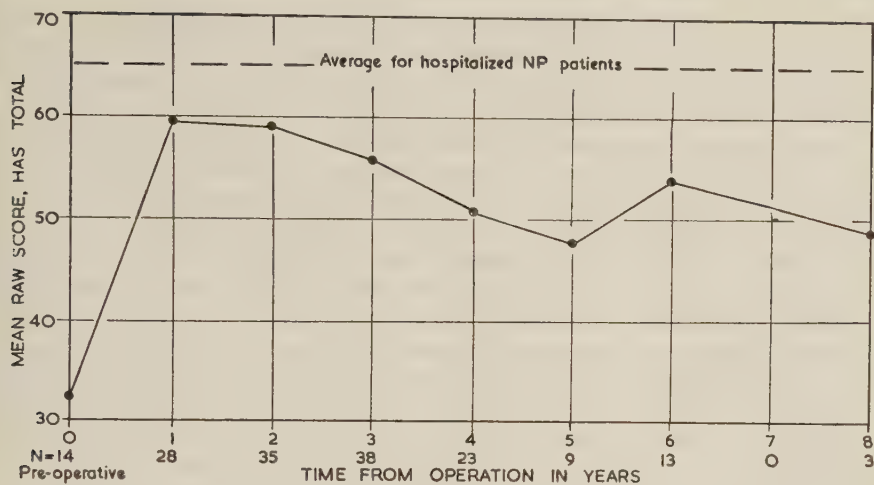


FIG. 4.—Mean HAS raw scores plotted against time after lobotomy*.

* The first year interval includes cases rated from 10½ to 15 months after surgery; the second year interval cases rated from 21 months to 30 months; the third year interval cases rated from 30 months to 42 months; and the same for years thereafter.

and work, activities, and recreation. Plots of these separate sub-scales against time after operation are not presented since in general they appeared to follow the same trend as does the total HAS score. The mean total raw score obtained by the 14 patients rated pre-operatively was 32.7. This is equivalent to the 21st percentile value for hospitalized psychiatric patients in general (9), and supports the view that the patients operated comprised an extremely ill group. Since the average raw score for hospitalized psychiatric patients (50th percentile) is 65, it appears from inspection of Figure 4 that the typical lobotomized patient did not attain a degree of improvement commensurate with the average of hospitalized psychiatric patients. Nevertheless, the trend indicated in Figure 4 does imply a rather marked general behavioural improvement following lobotomy.

3. Discussion of Findings Concerning Changes Following Lobotomy

Because exact statistical tests of the significance of changes in test scores were inappropriate, as indicated above, any conclusions which can be made concerning changes over time following lobotomy must be interpreted as being only tentative and suggestive. With this qualification, it seems possible to draw several interesting and pertinent generalizations from the data.

In the first place, it is noteworthy that most of the test results show a *decrement* in performance immediately after surgery—as reflected by testings 10 days after operation. This tendency no doubt is a function of the physiological trauma occasioned by the surgery itself: at this stage the patient is, primarily, an “organic” patient. This immediate effect appears to leave rather quickly, however, except in the case of the J-score on the CET, where it persists indefinitely up to the time of final measurement.

The test scores which appear to represent possibly real and substantial changes after lobotomy include, in addition to J on the CET, the Bender-Gestalt, Colour Naming, Digit Symbol, and Object Memory. It is difficult to evaluate the possible effects of practice on these tests, but it is noteworthy that

in each case the change was in the direction of improved performance. Further, the improved performance appears to have levelled off by the end of the first year post-operative. In most instances the point of highest performance occurs well before the end of the first year.

These general conclusions are similar to those reported by Scherer, Winne, Clancy and Baker (17, 18), who interpret their data to indicate that performance on tests measuring mental efficiency and organicity drop sharply during the first two-week post-operative period, then rise to reach a peak at about three months after surgery, and then gradually decline. Of the tests used in this study, the Bender-Gestalt, the CET, Object Memory, Colour Naming, and Digit Symbol all are probably somewhat sensitive to organic deficit. The test results in general suggest a greater mental efficiency and improved retentive functions after the immediate effects of the operation have disappeared. The one trend which cannot be fitted into this pattern is the J-score on the CET, which appears to reflect, rather, a persisting "organic-like" effect. As noted earlier, this trend may imply a lessened anxiety level. If so, the changes in retentive and attentive performances probably are due to the lessened anxiety rather than to any effects of the surgery on these functions *per se*. Indeed, we would be very hesitant to suppose that pre-frontal lobotomy has any *direct* beneficial effects on memory capacities, inasmuch as there is considerable evidence elsewhere that memory is hindered by physiological interventions in the frontal areas. Unfortunately, our test battery did not include any measures of anxiety: this, as seen in retrospect, was perhaps the most glaring inadequacy in the test battery used in this study.

The test instruments used, except for the Rorschach, were not particularly appropriate for evaluating any changes in overall personality structure. In the instance of the Rorschach test, as indicated in Figure 5, the indication is that no such changes occurred. This result, of course, may be due to the lack of validity

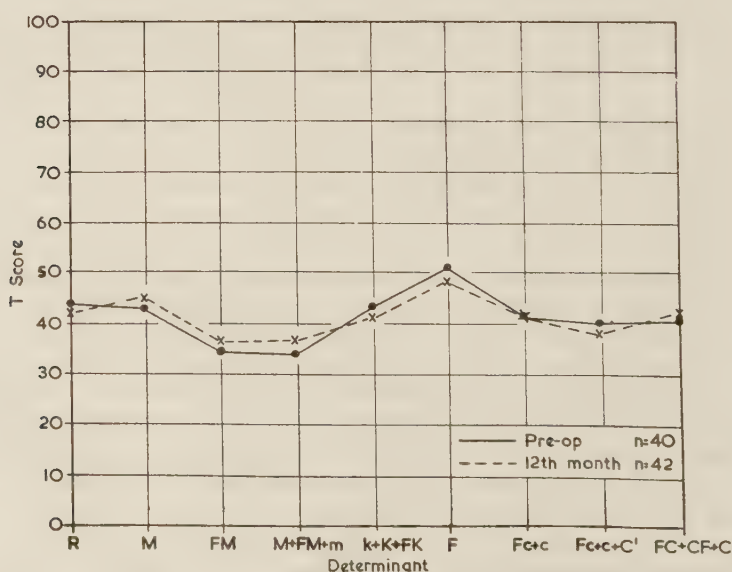


FIG. 5.—Rorschach psychograms of mean t-scores for pre-operative and one year post-operative testings.

of the Rorschach for this purpose. A more likely hypothesis, it seems to us, though, is that no overall personality changes did occur, i.e., that the effects of the operation were solely on the patients' mental efficiency—particularly retentiveness, attentiveness, and anxiety level—of the patients, without impinging directly upon their basic personality structures.

The HAS trend (Fig. 4) suggests an improved level of general, overall behavioural adjustment to the hospital ward living situations. In fact, the degree of improvement indicated is perhaps somewhat greater than would have been predicted on the basis of changes in test scores. If this is indeed the case, it may be due to changes in affect which were not measured by the tests used in this study.

V. THE RELATION OF HOSPITAL ADJUSTMENT SCALE SCORES AND CRITERION RATINGS

1. Findings and Discussion

Both the HAS and criterion ratings based on the patients' ward status were used as indices of general change after lobotomy. It should be interesting therefore, to see to what extent these two measures are related. It will be recalled that HAS ratings were obtained periodically on the patients whereas the criterion ratings were obtained only once, in November, 1955. It was not possible, therefore, to select very many instances in which the HAS and the criterion ratings were obtained at exactly the same period.

By making some allowances, however, 85 cases were obtained on whom both HAS and criterion rating scores were available. These allowances were that the HAS closest to a criterion rating was matched with that rating, provided it was within at least one year of it. All HAS ratings used in this analysis except one were made at least one year after operation—i.e. after a point at which the scores had presumably reached considerable stability. This one exception was made only six months after operation.

For the 85 cases the HAS scores were correlated with the criterion ratings, yielding the coefficients presented in Table III.

TABLE III
Correlations of HAS Scores with Criterion Ratings

	HAS Score						Correlation Coefficient	Level of Significance
Sub-scale I	..	..	..	..	..	..	.47	.01
Sub-scale II	..	..	..	..	..	..	.41	.01
Sub-scale III	..	..	..	..	..	..	.43	.01
Total	..	..	..	..	..	..	.52	.01

As noted in Table III all coefficients are positive and significant. Actually, the values probably are under-estimated somewhat, due to the fact that it was not possible to select data in such a way as exactly to match the times at which the two sets of measurements were obtained. The positive findings here increase one's confidence in the validity both of the HAS and the criterion ratings but have no other direct applicability to the lobotomy study.

VI. SUMMARY AND CONCLUSIONS

In May of 1951 a research project designed to evaluate prefrontal lobotomies by means of psychological instruments was inaugurated at the

Palo Alto Veterans Administration Hospital. Testing of lobotomy patients continued until April of 1955. During the intervening period 73 patients were examined.

The battery of psychological tests used included the Rorschach, the Rorschach Concept Evaluation Technique, the Draw-a-Person, a modified Porteus Maze, cards 4 and 7 of the Bender-Gestalt, Colour Naming, Digit Symbol, an Object Memory test, a Vocabulary test (Wechsler-Bellevue), a Sentence Completion test, and a test of Motor Inhibition. In addition behavioural ratings (Hospital Adjustment Scale) were obtained on many of the patients.

The testing programme was so arranged that certain of the tests were given at each of the following periods: pre-operative; and 10th day, 5th week, 3rd month, 6th month, and 1st year post-operative. The tests were administered by psychology trainees at this hospital. Many of the patients were unable to take some of the tests at certain prescribed testing periods: consequently the data available for analysis were not as great as would have been desirable, and systematic analyses of the data were not possible to as great an extent as could be wished. Nevertheless, the total amount of material gathered was very extensive, and certain generalizations can be drawn with considerable confidence.

The major purposes of the study were two: (1) to investigate the utility which those tests in the battery would have in predicting which of those patients operated would benefit maximally from the operation; and (2) to learn something about the course of changes in psychological functions which would occur following lobotomy.

With regard to the first of these questions—the predictive ability of the psychological tests—it was, of course, necessary to have some criterion of patient improvement against which to evaluate the tests. The major such criterion used was a rating based on the placement of the patients as of November, 1955. This rating varied from 0 (minimal or no improvement, patient on disturbed ward) to 4 (patient at home and working or capable of work).

When the test scores obtained by the patients pre-operatively were compared with the criterion ratings obtained by the patients in November of 1955 (this was at least one year post-operative for all patients) it was found that the relationship was statistically significant for only one of the tests (Rorschach Concept Evaluation Technique). That is, for the sample studied, all of the other tests used failed to show significant predictive validity as to which patients would benefit most from lobotomy. This finding should not be taken to mean that these tests are necessarily not useful in selecting patients for lobotomy, but rather that *after patients have already gone through careful screening for lobotomy* the use of these tests does not appear to add any significant predictability.

As to the second question—concerning changes in patients following lobotomy, as measured by the tests used in this study, the data indicated that most psychological functions measured tend to decline immediately following lobotomy—during which period the patient gives a rather typical “organic” picture—then to rise gradually with the optimal improvement apparently reached before the end of the first year post-operative. The improved functions appear to be chiefly in mental efficiency and retentive functions. It is also hypothesized that there is a significant decrement in level of anxiety, though our results did not bear directly upon this question. It is our hunch that the apparent improvements in retentive functions is in fact due to a lessening of anxiety rather than to any direct effect of the operations on retentive capacities.

Our evidence indicates that prefrontal lobotomy did not bring about basic personality change. This tentative conclusion is based on the fact that Rorschach psychograms were not changed appreciably by operation.

The Hospital Adjustment Scale data indicated that, in general, the behavioural adjustment of operated patients—when considered as a group—improved rather dramatically during the first year post-operative, and then declined slowly thereafter. The improvement never reached the average for hospitalized neuropsychiatric patients in general, but at the same time the improvement, such as it was, was maintained to at least some degree for at least eight years post-operative.

The major findings of this study may be stated briefly as follows:

1. Scores of the one variable (J) of the Rorschach Concept Evaluation Technique given pre-operatively correlated significantly with the rated clinical status of the patients a year or more after operation; other test scores failed to show any significant correlations with the criterion.

2. After operation there was a tendency for test scores reflecting attentive and retentive capacities to decline, then to rise slowly to beyond the pre-operative level: these improved functions are interpreted as being due to a decrement in anxiety level, and

3. Behavioural adjustment scores (Hospital Adjustment Scale) tended to rise up to one year post-operative, and then to decline slowly.

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MENTAL DISEASES IN PEKING BETWEEN 1933 AND 1943

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THIS report is based on a survey of 1,716 Chinese patients admitted to the Peking Municipal Psychopathic Hospital during the years 1933-1943. It is mainly concerned with a statistical presentation of the relative frequency of the various mental disorders and with certain other data which may be of interest to psychiatrists and other members of the medical profession.

As early as 1912, Peking already had an asylum for the custodial care of insane patients (3, 16). Towards the end of 1933, the Peking Union Medical College, after negotiation with the Municipal Health Department, undertook the re-organization of the asylum into a Municipal Psychopathic Hospital, which for some years was the institute for teaching neuropsychiatry to medical students. Because of limited bed capacity, the number of patients cared for at any one time rarely exceeded 300. From the re-organization of the Hospital in 1933 up to the end of 1943, a total of 1,808 patients were admitted. Of these patients, 18 were foreign nationals and 71 had no or incomplete records, leaving 1,716 cases available for the present study.

This paper is based on work done between 1942-1944 when the authors were resident psychiatrists in the Peking Psychopathic Hospital.

PRESENTATION OF STATISTICAL DATA

Sex and Age. Among the 1,716 patients, 1,052 were men and 664 women, giving a ratio of about 3 males to 2 females.

The age of these patients at the time of first admission ranged from 11 to 73 years, with an average of 33.5. With a few exceptions, the patients were admitted within two years of the onset of illness. The age distribution of the patients is given in Table I. About two-thirds of them were young adults between 20 and 40 years of age. Patients over 50 years of age constitute only 9.8 per cent. of the total. Both male and female patients have practically the same age distribution.

Birthplace and Race. The majority of the patients before admission were residents of Peking or its vicinity. Enumeration of the native provinces of these patients showed that 83.8 per cent. of them came from North China and 14.1 per cent. from South and Central China. In 2.1 per cent. of the cases, these data were lacking. It is interesting to note that according to the census by the Municipal Police Department in 1941 (20), barely 4 per cent. of the residents of Peking came from provinces in South and Central China, yet 14.1 per cent. of our patients had their native homes in these provinces.

TABLE I
Age Distribution of the Mental Patients

Age Groups			Total		Males		Females	
			No.	Per cent.	No.	Per cent.	No.	Per cent.
10-14	..	..	3	0.2	2	0.2	1	0.2
15-19	..	..	92	5.4	62	5.9	30	4.5
20-24	..	..	302	17.6	198	18.8	104	15.7
25-29	..	..	334	19.5	206	19.6	128	19.3
30-34	..	..	303	17.6	187	17.8	116	17.5
35-39	..	..	205	11.9	118	11.2	87	13.1
40-44	..	..	160	9.3	91	8.7	69	10.4
45-49	..	..	135	7.9	82	7.8	53	8.0
50-54	..	..	80	4.7	51	4.8	29	4.4
55-59	..	..	57	3.3	33	3.1	24	3.6
60-64	..	..	17	1.0	10	0.9	7	1.1
65 and over	..	..	14	0.8	7	0.7	7	1.1
Unknown	..	..	14	0.8	5	0.5	9	1.3
Total	..	..	1,716	100.0	1,052	100.0	664	100.0

As to racial classification, 1,233 patients were Chinese, 119 Manchus, 15 Mohammedans (Central and West Asian origin) and 4 Mongolians. In 345 cases this information was not recorded.

Agencies Sending Patients to Hospital. The agencies responsible for sending patients to the hospital are given in Table II. At first, the patients were committed chiefly by the police, but later on more patients were sent in by their relatives for hospitalization and treatment.

TABLE II
Agencies Sending Patients to Hospital

Agencies								No.	Per cent.
Family	..	..	..	..	..	..	..	822	47.9
Police	..	..	..	..	..	..	..	745	43.4
Public institutions	..	..	..	..	..	..	..	132	7.7
Not recorded	..	..	..	..	..	..	..	17	1.0

Diagnostic Classification. The diagnoses are grouped according to the Condensed Classification of the American Psychiatric Association (18). Both number and percentage of the various types of psychosis among the 1,716 patients are shown in Table III overleaf.

As shown in the table, schizophrenia ranked first, including nearly one-third of the total admissions. Manic-depressive psychosis with 22.1 per cent. was second. General paresis, psychoses with psychopathic personality, epileptic psychosis, psychosis with other infectious diseases, psychoneurosis, psychosis with mental deficiency, etc., then followed closely one another. Certain psychoses showed notable sex differences. Among male patients, general paresis, psychosis with other infectious diseases, alcoholic psychosis and epileptic psychoses had higher percentages as compared with female patients. The females had a higher incidence in senile psychosis, involutional psychosis, psychosis due to other metabolic diseases and manic-depressive psychosis.

Race and Types of Psychoses. A study of racial difference in the incidence of various types of psychoses is not very reliable because the number of cases in the present survey is small. However, Kao, Ting and Hsu (7), reporting on a

TABLE III
Classification of the Diagnoses

Diagnoses	Number			Percentage		
	Total	Male	Female	Total	Male	Female
With Psychoses:	1,660	1,017	643	96.7	96.7	96.8
1. Psychoses with syphilitic meningo-encephalitis (general paresis)	125	104	21	7.3	9.9	3.2
2. Psychoses with other forms of syphilis of central nervous system	6	4	2	.3	.4	.3
3. Psychoses with epidemic encephalitis	17	9	8	1.0	.9	1.2
4. Psychoses with other infectious diseases	71	55	16	4.1	5.2	2.4
5. Alcoholic psychoses	21	20	1	1.2	1.9	.1
6. Psychoses due to drugs or other exogenous poisons	7	3	4	.4	.3	.6
7. Traumatic psychoses	3	3	0	.2	.3	0
8. Psychoses with cerebral arterio-sclerosis	17	11	6	1.0	1.0	.9
9. Psychoses with disturbance of circulation	4	2	2	.2	.2	.3
10. Psychoses with convulsive disorders (epileptic psychoses)	82	64	18	4.8	6.1	2.7
11. Senile psychoses	28	11	17	1.6	1.0	2.6
12. Involutional psychoses	25	6	19	1.4	.6	2.9
13. Psychoses due to other metabolic diseases, etc.	22	8	14	1.3	.8	2.1
14. Psychoses due to new growth	1	1	0	.1	.1	0
15. Psychoses associated with organic changes of the brain	5	4	1	.3	.4	.1
16. Manic-depressive psychoses	380	189	191	22.1	18.0	28.8
17. Dementia praecox (schizophrenia)	559	340	219	32.6	32.3	33.0
18. Paranoia and paranoid conditions	39	30	9	2.3	2.8	1.3
19. Psychoses with psychopathic personality	84	53	31	4.9	5.0	4.7
20. Psychoses with mental deficiency	60	39	21	3.5	3.7	3.2
21. Undiagnosed psychoses	37	26	11	2.2	2.5	1.6
Without Psychoses:	56	35	21	3.3	3.3	3.2
22. Without psychoses	44	29	15	2.6	2.7	2.3
23. Psychoneuroses	67	35	32	3.9	3.3	4.8
24. Primary behaviour disorder	12	6	6	.7	.6	.9
Grand Total	1,716	1,052	664	100.0	100.0	100.0

smaller number of patients, came to the conclusion that there is a definite relative increase in the ratio of parergastic psychosis (schizophrenia) to manic-depressive psychosis in the Manchus as compared with Chinese patients. We have made a comparison between Chinese and Manchu patients with reference to the two most frequent psychoses to see if there is any significant difference.

TABLE IV
Incidence of Schizophrenia and Manic-depressive Psychosis Among Chinese and Manchu Patients

Race				Schizophrenia	Manic-depressive Psychosis	Total
Manchu	..	..	..	34	19	53
Chinese	..	..	..	414	280	694
Total	..	..	..	448	299	747

$\chi^2=0.34.$

Among 1,233 Chinese patients, there were 414 cases (33.6 per cent.) of schizophrenia and 280 cases (22.7 per cent.) of manic-depressive psychosis (ratio of schizophrenia to manic-depressive psychosis—1.48:1). Among 119 Manchu patients, there were 34 cases (28.6 per cent.) of schizophrenia and 19 cases (16.0 per cent.) of manic-depressive psychosis (ratio of schizophrenia to manic-depressive psychosis—1.79:1). Though the percentage of schizophrenia among the total admissions was higher among Chinese patients, yet the ratio of patients with schizophrenia to those with manic-depressive psychosis was slightly higher among the Manchus. However, if we evaluate the significance of the difference by the χ^2 test (4), χ^2 is found to be only 0.34 (with χ^2

below 4, the observed difference is generally not considered as statistically significant). Hence, the result does not support the view that schizophrenia is more common among Manchus.

Outcome of Hospitalization. The fate of the patients up to the end of 1943 is shown in Table V. Because of shortage of beds, most of the patients, after a period of observation and treatment, were discharged to the care of their families even though there might have been no definite improvement in their mental condition. Among our patients, 220 had one or more re-admissions (15.7 per cent. of total discharges). Though the majority of the patients were young adults, 14.5 per cent. were known to have died while in the hospital or shortly after discharge. The most common causes of death were pulmonary tuberculosis and bacillary dysentery.

TABLE V
Outcome of the 1,716 Patients at the End of 1943

	Outcome						No.	Per cent.
Discharged	..	..	..	..	..	..	1,400	81.6
Recovered	..	..	..	..	..	..	194	11.3
Improved	..	..	..	..	..	..	667	38.9
Unimproved	..	..	..	..	..	..	539	31.4
Died	..	..	..	..	..	..	249	14.5
Still in hospital	..	..	..	..	..	..	67	3.9
Total	..	..	..	..	..	..	1,716	100.0

DISCUSSION

Though mental diseases in China are essentially the same as in western countries, as observed by a number of neuropsychiatrists (1, 8, 11, 12, 15, 16, 19), racial and cultural differences may give rise to difference in the relative prevalence of various types of mental disorders. In the following, comparisons will be made chiefly with statistics from the United States, because the American classification was in general use in Peking at that time and consequently the data are more readily comparable.

The most notable difference between this group of patients as compared with similar groups in the United States (2.9) is that our patients consisted of considerably fewer persons of old age. The average age at the time of first admission among our patients was 35.5 years, while that of the patients admitted to the mental hospitals in New York was 45.5 years (9). In our data, patients over 50 years of age constituted only 9.8 per cent. of the total, while in the American statistics such patients amounted to 37.5 per cent. As the incidence of mental diseases is known to be higher in the older age groups, one would expect that there would be proportionately more old people among the mental patients than in the general population. However, the census of Peking in 1941 (20) showed that 14.3 per cent. of the city's population were over 50 years of age. Thus, there were fewer old people among our patients than in the population. Apparently many patients of advanced ages did not come to the Psychopathic Hospital.

There was a strikingly low percentage of senile and arteriosclerotic psychoses among our patients. In our data, these two groups of psychoses amount to only 2.6 per cent. of the total, while statistics from New York and Massachusetts give 22.2 per cent. and 18.6 per cent. respectively (2.9). That

in China fewer people live to old age and that arteriosclerosis is supposed to be less common here can partly account for the low percentage of these psychoses. However, the main reason is probably due to the fact that those people who did live to the age at which these degenerative diseases occur were not uncommonly leading an easy life at home, being taken care of by their children. Some degree of queerness and disorderly conduct could usually be tolerated. Moreover, some people would consider it a disgrace to the family if they sent their elderly people to the mental asylum. A large number of these patients probably remained in the care of their families.

Numerically, schizophrenia is the leading category in this series of cases, followed by manic-depressive psychosis. These two "endogenous" psychoses together comprise over one half of the total cases. This is attributable to the fact that these diseases commonly attack young adults who constituted the bulk of our patients. As in most hospital statistics, the percentage of schizophrenic cases is considerably higher than that of manic-depressive psychoses. However, in some published reports from Canton (6, 10) more patients were diagnosed as having had manic-depressive psychoses than schizophrenia. This has been explained by the difference in the temperament of the Southerners favouring the development of affective psychoses (16). Possibly a difference in diagnostic criteria may be responsible for this discrepancy.

General paresis, with 7.3 per cent. of the total admissions, ranked third in the list. Though earlier writers gave the impression that this disease was rare in China, reliable statistics certainly did not support this point (5, 14). Many cases in the present series belonged to the classical "expansive" type. Only a small number of the patients had a history of having had arsenical treatment in the past. It is to be noted that this disease occurs four times more frequently among male than female patients.

There are 17 cases of psychoses with epidemic encephalitis in our series. This type of psychosis has seldom been reported from other parts of China. Alcoholic psychosis which constitutes about one-tenth of psychiatric patients in America comprised only 1.2 per cent. of our patients. The incidence of this disease is not high in other parts of China (10, 16) or in Japan (13).

In China the taking of alcoholic drink was most unusual except as part of a meal, but whether the difference in incidence of alcoholic psychosis is due to this, or to a higher tolerance, or to the possibility that the amount of alcohol consumed seldom reached the quantity required to produce deleterious change in the central nervous system is not known. In the present series, other cases of psychosis due to intoxication were all, with the exception of one following carbon monoxide poisoning, the result of addiction to opium. Though opium addiction was not uncommon in China, mental disorders attributable to this drug habit were not frequently seen. Epileptic psychosis with 4.8 per cent. of the total admissions had a somewhat higher percentage as compared with American statistics.

Since an unknown number of mental patients in the city did not come to the Psychopathic Hospital, it is not possible to estimate the incidence (annual rate of new cases) or prevalence (number of patients in the population) of mental diseases in Peking from the hospital data alone. Although without a careful survey the prevalence rate cannot be obtained with any reliability, two estimates have so far appeared in the literature. Gamble (3) stated in his book on Peking that the police gave the number of insane as 1,366 when the city's population was 811,556 in 1920, giving a prevalence rate of 168.3 per 100,000 population. McCartney (11), basing on hospital reports and answers to inquiries, estimated

that there were 1,341,600 insane persons in China. Taking the population of China as 400 million, the prevalence rate would be 335.4 per 100,000. The rate for the United States in 1936 was 335.3 (9), while in Japan the rate in 1935 was 120.4 (17). In spite of this there are reasons for believing that there are relatively fewer mental patients among the populace in China. Firstly, since the life expectancy of the Chinese people is generally considered to be shorter than that of the Americans or Europeans and since mental diseases occur more frequently among people of the older ages, the Chinese people with fewer old persons will naturally have a lower incidence of mental diseases. Secondly, for want of proper management, insane persons in China died off more quickly than patients kept in well-equipped mental hospitals in the West. Even if we assume a very low prevalence rate of 100 per 100,000 population, there would be about 2,000 mental patients in Peking, a number far exceeding the accommodation of the Psychopathic Hospital at that time. The majority would have had to be cared for in their own homes.

SUMMARY

In a survey of 1,716 mental patients admitted to Peking Municipal Psychopathic Hospital between the years 1933 and 1943, it has been shown that the patients were composed of relatively more young adults and fewer old people as compared with similar groups of patients in the United States. Schizophrenia, comprising 32.6 per cent. of the total admissions, headed the list. Manic-depressive psychosis with 22.1 per cent. ranked second, followed by general paresis, psychosis with psychopathic personality, epileptic psychosis, etc. In contrast to the high incidence of senile and arteriosclerotic psychosis in the western countries, these two diseases together amounted to only 2.6 per cent. of our cases. Probably many such patients remained in the care of their families. Alcoholic psychosis which has a high incidence in America was infrequently encountered. Epileptic psychosis and psychosis with other infectious diseases seem to have had somewhat higher percentages.

It was estimated that the Psychopathic Hospital could accommodate only a small percentage of the mental patients in Peking. Due to shortage of hospital beds, many of those who had been admitted had to be discharged to the care of their families, even without improvement in their mental conditions. Among the patients in this survey, only 11.3 per cent. were considered as having recovered from their mental illness and among those discharged from the hospital, 15.7 per cent. had one or more re-admissions. During the ten years covered by the present study, 14.5 per cent. of the patients are known to have died. Since an unknown number of patients never came to the Psychopathic Hospital, the incidence or prevalence rate of mental diseases in Peking during the time in question cannot be estimated on the data herein presented.

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VARIATIONS IN SKIN RESISTANCE AND THEIR RELATIONSHIP TO G.S.R. CONDITIONING

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ANY particular system which is being conditioned is likely to maintain a certain level of background activity throughout the experimental procedure; either of a discontinuous nature, as, for example, with eyeblink, heart rate and respiratory cycle, or continuously, as in the case of basal skin resistance and muscle tonus.

This background activity or level of arousal does not remain constant but usually varies in time, presumably as a result of underlying neural excitation or inhibition. It may increase throughout an experiment if the subject becomes highly motivated, as with the gradients of muscle action potentials observed by Bartoshuk (1955), or decrease, if the subject becomes more relaxed and familiar with the set-up, as Duffy and Lacey (1946) found with level of skin conductance.

The activity of a system which is being investigated may be measured in a number of ways, e.g. in *level* of skin resistance, in *frequency* and *amplitude* of cardiac output, or in the *number* of spontaneous eyeblinks during inter-trial periods. Little attention has been given to such matters; surprisingly so, since it seems important for a number of reasons to consider the excitability or general reactivity of the specific system which is being conditioned.

The actual state of underlying neural excitation may, of course, be only imperfectly measured by existing techniques, and this is a difficulty which must be faced (and will be discussed later); on the other hand, even if neural activity is fairly represented in the measures taken, the subjects will not all necessarily express their arousal via the same system (cf. the work by Lacey *et al.* (1953) on response specificity, and that of Malmö and Shagass (1949) on symptom specificity).

It is the purpose of the present paper to draw attention to some of the major variations in skin resistance which occur during GSR conditioning, and to discuss their importance and relationship with the measures of conditioning. The variations which were considered were as follows:

- (i) Basal level of skin resistance.
- (ii) Number of spontaneous variations.

Third, relationships between amplitude of the UCR and associated pre-stimulus levels were investigated.

PROCEDURE

Full details of the experiment and apparatus have been given elsewhere (Martin, 1959). To recapitulate the procedure briefly, the palm to palm skin resistance of 23 normal male subjects was measured throughout the conditioning procedure, using a very small constant current of 10 μ A. Subjects were conditioned to a dim light (CS) in association with a 980 c.p.s., 110 db. tone (the

UCS) with a CS-UCS interval of 5-seconds. Intervals between the 13 reinforced trials varied from $\frac{3}{4}$ minute to $2\frac{1}{4}$ minutes.

Initial trials of the CS were given to ensure adaptation to this stimulus. Subsequent acquisition of the CR was very rapid and was stably maintained. Thirteen extinction trials followed.

Introversion and neuroticism scores were obtained for each subject by means of a questionnaire which has been previously used a great deal in Eysenck's dimensional programme (Eysenck, 1957). Following his line of argument it was predicted that introverts would condition more readily than extraverts; no significant relationship between neuroticism and conditionability was expected.

RESULTS

1. *Basal Skin Resistance.* Level of skin resistance usually showed a slight rise during the pre-conditioning adaptation trials but invariably dropped by a very great amount following the first UCS. After this there was a slight tendency to recover, but as a rule the level of skin resistance then remained fairly steady until the end of the experiment.

Two measures of mean resistance were calculated for each subject; the first (BSR₁) was based on the level immediately preceding each UCR and is therefore derived from 13 readings. Since the level prior to the first UCS was in some cases extremely high, whereas the remaining twelve did not vary so greatly, a second mean was obtained (BSR₂), based on the 12 pre-stimulus readings of UCRs 2-13, that is, after the sudden large drop in basal skin resistance to the first UCS. In fact, both means correlate significantly with the number of CRs given by the subject, as can be seen from Table I. The correlations are negative, and show that when basal skin resistance is high (i.e. when

TABLE I

Correlations Between Mean Basal Skin Resistance and Number of Conditioned Responses

	r	N
BSR ₁ (based on mean of 13 pre-UCR readings) and CRs	-0.5429*	23
BSR ₂ (based on mean of 12 pre-UCR readings) and CRs	-0.5553*	23

* Significant at the 1 per cent. level.

sympathetic activity is low) conditioning is less; conversely, when skin resistance is low a greater number of conditioned responses are given.

This is an interesting relationship, for many autonomic measures—in particular that of palmar sweat gland activity—have been shown to vary quite closely with the level of the subject's arousal (Duffy, 1957). During relaxation or sleep, autonomic activity is reduced, but it is very high during alert, excited states. Insofar as basal skin resistance is an index of arousal (the point will be discussed below) it appears that subjects who are more relaxed do not condition as well as those who are fully aroused and alert.

2. *Spontaneous Responses.* Some subjects produced many spontaneous responses, others practically none. Two typical examples of this are reproduced in Figure 1. Any fluctuation in basal skin resistance greater than 2 kilohms was counted as a spontaneous response, and the total number of such responses given during acquisition was correlated with the number of conditioned responses given. This correlation was very high (+0.62) and significant beyond the 1 per cent. level.



FIG. 1.—Two records obtained during acquisition, illustrating the differences between subjects in the occurrence of spontaneous responses.

What is the origin of this type of response? Mundy-Castle and McKiever (1953) drew attention to them and suggested that they arise through lack of cortical inhibition of lower autonomic centres. There is no direct experimental evidence in support of this, and the possibility that they are spontaneous discharges from end organs should not, perhaps, be ignored. More spontaneous responses occur when skin resistance is low: the correlation of -0.487 obtained in the present study is significant at the 5 per cent. level. Lacey and Lacey (1958) found a negative and similarly significant correlation between the two variables in one of their two samples, but not in the other.

These authors incline to the view that "level of tonus" and frequency of spontaneous responses are independent variables, a conclusion which seems premature in the light of the present evidence.

3. *Relationship of UCR Amplitude to Basal Levels.* There is hardly any need to draw attention to the close relationship which has been observed between GSR amplitude and pre-stimulus levels, nor to the statistical ingenuity which has been spent on the problem. The size of the relationship varies greatly from sample to sample, but it has also been shown to decrease considerably within a single study involving successive responses. Martin (1960) found in an experiment on GSR adaptation that the size of the correlation between

GSR amplitude and basal levels was very high for the first response but zero by the twentieth response.

Correlations were therefore calculated between amplitude in kilohms of unconditioned and conditioned responses, and their associated pre-stimulus levels, throughout the acquisition procedure. The results are given in Table II.

TABLE II

Correlations Between Amplitude of UCRs and CRs and Pre-stimulus Levels of Basal Skin Resistance

						<i>r</i>	<i>N</i>
UCR ₁ and BSR	..	..	..	..	..	+0.9220†	23
UCR ₆ and BSR	..	..	..	..	..	+0.8257†	23
UCR ₁₃ and BSR	..	..	..	..	..	+0.2603	23*
CR ₃ and BSR	..	..	..	..	..	+0.4734‡	23*
CR ₁₀ and BSR	..	..	..	..	..	+0.3138	23*

* Only 20 of the subjects gave a response in these groups, but correlations were calculated on the total *N* of 23.

† Significant at the .1 per cent. level.

‡ Significant at the 5 per cent. level.

The size of the correlation drops in a very clearcut way, the first being highly significant, and the last failing to reach statistical significance.

Table II also gives correlations between two of the conditioned responses (CRs 3 and 10) and their skin resistance levels. These are both small and of borderline statistical significance.

The size of the first UCR during acquisition was in every case the largest given by the subject. Auditory thresholds were obtained prior to the conditioning experiment, and they were found to fall within a very narrow range, so that differences between subjects in responsiveness to the first UCS could not be attributed to differences in receptor sensitivity. It seems unlikely, moreover, that this factor could account for the greatly differing effects that sudden, startling tones or noises have upon individuals with normal hearing, such that they are ignored by some but produce violent reactions in others.

It is reasonable to suppose that the size of the first UCR measures the subject's reaction to the first UCS, and it is obviously important to consider whether there are any individual differences in this connection. For varying the intensity of the UCS in a conditioning experiment changes level of drive, and this, theoretically, should affect the degree of conditioning. Lacey's (1956) formula was applied to these data, to ascertain whether a given subject's first UCR was *greater* or *smaller* than that which would be predicted from his pre-stimulus level of skin resistance, and the resulting autonomic lability scores were then correlated with the number of CRs given during acquisition. The resulting coefficient was -0.2218 , which was not significant but in the predicted direction*, i.e. subjects giving comparatively larger UCRs were those giving more conditioned responses.

DISCUSSION

There is ample evidence that palmar skin resistance varies with the level of sympathetic nervous system activity and with the subject's central state of arousal (Kleitman, 1939, Richter, 1926), but there is also evidence to suggest

* Skin resistance was measured in kilohms; skin resistance decreases following a stimulus so that low autonomic lability scores in this case indicated a greater reaction to the tone. The correlation between autonomic lability scores and number of conditioned responses was, therefore, negative in direction.

that the state of the end organs may be modulating the measurement of neural impulses (Davis, 1930; Davis *et al.*, 1955).

The significant negative relationship between level of skin resistance and number of conditioned responses may, therefore, show that conditioning of this modality is partly a function of arousal, but it may also point to an *increase in threshold at the periphery* during high skin resistance, whereby weak impulses which under other conditions would produce a CR are not able to excite the end organs into making a response. When skin resistance is high the peripheral sweat gland cells are highly polarized and may be more difficult to activate. The important point to emphasize is this: if end organ involvement is considerable, then the *same number of neural impulses passing along autonomic nerves may produce a CR in one subject but not in another*.

Presumably another kind of threshold is reached in cases of extremely low skin resistance, where local sweat glands are so highly active that further responsiveness even to strong stimuli is difficult to achieve. This factor was not marked in the present experiment, but it has been very clearly observed in subsequent studies which have been carried out during very warm weather. Obviously, these are important problems to resolve in order to maximize the effectiveness of skin resistance measures as indicators of *central* change. Malmö (1958) has recently argued for the use of measurements of physiological activity as indicators of drive level, and this offers a singularly promising lead in the problem of assessing strength of drive. His thoughtful paper should be consulted, for it deals with a number of relevant experimental findings and theoretical issues in this connection.

As with basal skin resistance, so spontaneous responses may be central in origin, or, conceivably, discharges occurring at a lower level. Lacey and Lacey (1958) have discussed these responses at length. They argue that such autonomic responses act as stimuli which feed back to energize the cortex, and that "episodes of autonomic discharge may be paralleled by episodes of changes in cortical arousal, whether the autonomic discharge is spontaneous or stimulus evoked". Both sets of variations, autonomic and cortical, may, they suggest, be produced by the same neural mechanisms.

There is a great deal of individual variation in the number of spontaneous responses given, some subjects producing many and others hardly any at all. Most subjects give the greatest number after the first and second unconditioned stimuli, after which there appears to be a decrease in their occurrence. If these spontaneous responses act as stimuli to energize the cortex, as Lacey and Lacey argue, they may be considered as drive stimuli in the sense that this term is used in current learning theory (Estes, 1958).

The overall evidence is not clear concerning the relationship of spontaneous responses to basal levels of skin resistance. The correlation between number of spontaneous responses and conditioned responses is very significant; it is paralleled in an interesting way by the results of Willett (1960) who observed correlations, not quite significant at the 5 per cent. level, between number of spontaneous eyeblinks and eyeblink conditioning to a tone followed by a puff of air.

The activity level of the system being conditioned seems, therefore, to play some part in the conditioning process, although this part may be more or less important in the different modalities. It is a factor which has been undeservedly neglected, particularly in theories which are concerned with individual differences. A given subject may not condition well in a particular modality simply because his general "activity" or "arousal" of responsiveness

to stimuli is *not expressed in that system*. It might, therefore, be necessary to condition several systems before reaching a justifiable conclusion that a subject could not be conditioned.

The results also have implications for general theories of learning. In the basic Hullian equation, drive acts on habit strength to produce learning, and it is accepted that one of the ways to vary drive level experimentally is to vary the intensity of the UCS (Spence, 1958). A *standard* UCS is likely to affect subjects differently for a number of reasons (Eysenck, 1960). One is the differences in subjects' receptor threshold, but in addition to this there are differences between subjects in central reactivity, especially to sudden and startling noises. This factor was taken into account in the present experiment by calculating autonomic lability scores and correlating these scores with the number of conditioned responses. The resulting r was not significant (the number in the sample was only 23) but it was in the predicted direction, and partially supports the expectation that those subjects who react greatly to the UCS are those who condition well.

These findings should be repeated before firm arguments are based on them, for, regrettably, many of the results in this field do not accord with one another. But if they are valid, some consequences arise which are especially relevant to theories which attempt to deal with individual differences in behaviour.

One such theory is that proposed by Eysenck (1957), and one of the specific predictions arising from this theory is that introverts will, among other things, condition more rapidly because excitatory potential is dominant in this type. So far most of the work carried out in this connection has been with eyeblink conditioning. As Eysenck has himself pointed out on many occasions, there are undoubtedly a large number of factors operating in any given experiment which could attenuate the observed correlations between the personality measures and conditioning. In the first place the criterion of "introversion", which depends upon questionnaire measurement, is unsatisfactory in many ways. Not only this, but, as the present results show, it may be unwise at the present time to depend too heavily upon results from one particular type of conditioning. The correlations obtained in the present study between number of CRs and introversion (as well as between CRs and neuroticism) were very low and non-significant; but there are many other, and possibly more relevant, measures of conditionability which might be used in this connection, and this aspect of the experiment will be followed up in subsequent studies using larger groups.

Again, it needs no emphasis that theories within psychology at the present time are not highly organized systems, and one of the consequences is that they generate only weak and imprecise hypotheses for experimental test. Their value in stimulating and directing experiments cannot be denied, but there are clearly some urgent experimental problems ahead. One is to determine how widely the generalizations of learning theory hold, and to specify the conditions under which such general laws as there may be will operate.

SUMMARY

1. Level of basal skin resistance was measured continuously throughout the conditioning procedure and was found to correlate negatively and significantly with the number of CRs given by the subjects. Two explanations were considered: the first, that conditioning relates to level of arousal, the second

that there is an increase in threshold at the periphery during high resistance such that CRs are less likely to occur.

2. Spontaneous responses were counted throughout acquisition: they correlated positively and significantly with the number of CRs produced. It was suggested (a) that they were probably central but possibly peripheral in origin, and (b) that they might act as cortical energizers.

3. Correlations between amplitude of UCRs and basal level diminished throughout acquisition. The amplitude of the first UCR was considered to indicate degree of responsiveness to the UCS. On the hypothesis that different amplitudes might reflect differences in drive level produced by the UCS, autonomic lability scores were calculated, and correlated with number of CRs given by each subject. The resulting coefficient was in the predicted direction, but was not statistically significant.

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"TEMPOSIL" A NEW DRUG IN THE TREATMENT OF ALCOHOLISM

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INTRODUCTION

In the last decade the use of disulfiram (Antabuse) has considerably altered the treatment of chronic alcoholism. However, unpleasant side-effects of headache, metallic taste in the mouth, abdominal discomfort and impotence are found in patients on maintenance treatment with this drug and deters them from taking it (4, 10). Alcohol-disulfiram reactions can be accompanied by cardiac complications or sudden death (9, 11). Despite these difficulties alcoholics who take disulfiram regularly have better abstinence records than those who do not (15). Many reasons may be postulated for these results, but we have regarded the use of disulfiram as a means of providing a period of "forced" abstinence while the alcoholic is readjusting to the demands of resuming his job, family relations, etc. During this time some insight and understanding of the nature of his difficulties may be established. The remainder of this paper describes the investigation of a new substance, Temposil, which produces a similar effect to disulfiram.

Temposil was first described by Ferguson (5). It is essentially the calcium salt of carbimide, an industrial product long known for its ability to produce "mal rouge" in workmen exposed to it if they later drank alcohol. For medical use a highly purified preparation of carbimide is required with the addition of sufficient acid to the calcium carbimide to neutralize it and keep the pH of the medium between four and five. This is achieved by adding citric acid 2 parts by weight to one part of calcium carbimide.

As rapid absorption of carbimide from the stomach produces unpleasant direct effects on the C.N.S. the final tablet form used was of a "slow release" type.

MODE OF ACTION

During the oxidation of ethyl alcohol acetaldehyde is produced. In normal human blood acetaldehyde is present in amounts of less than 0.05 mg. per 100 c.c. but after drinking alcohol blood acetaldehyde levels rise to 0.2-0.4 mg.

per 100 c.c. If a patient has previously had disulfiram or Temposil, after drinking alcohol blood acetaldehyde levels are markedly increased because these substances appear to inhibit enzymes needed for the oxidation of acetaldehyde (7, 8, 12, 13).

The effects of disulfiram were thought to be due only to increased blood acetaldehyde concentrations, but there is evidence to show that both disulfiram and Temposil alter the vascular reaction to acetaldehyde (5, 6, 12).

METHOD OF INVESTIGATION

Patients treated with Temposil had been admitted to the alcoholic unit, St. Luke's Hospital, Middlesbrough and were chronic alcoholics within the definition of the World Health Organization Memorandum (1950) on this subject. They ranged in age from 23–59 years with an average age of 40. Thirty male and 3 female patients were treated during this investigation.

Before commencing treatment the following investigations were carried out:

1. Full physical examination.
2. Full blood count and film.
3. Urinalysis.
4. Liver function tests:
 - (a) Plasma alkaline phosphatase.
 - (b) Thymol turbidity.
 - (c) Van Den Bergh reaction.
 - (d) Total plasma bilirubin.
 - (e) Urine for urobilinogen, urobilin and bilirubin.
5. Chest X-ray.
6. Some ten patients in the later stages of the investigation had E.C.G. recordings.

All the cases treated were in good health with normal laboratory findings at the time of the test reaction.

As in other investigations reported at that time initially patients were given Temposil in a dose of 50 mg. daily (1, 2, 14). At a later stage for reasons discussed below a dosage of 100 mg. of Temposil was used.

The technique adopted for each test reaction was as follows:

The patients were encouraged to take their ordinary meals before tests and as far as possible every attempt was made to minimize the artificial atmosphere associated with drinking in hospital. The alcohol used was always that of the patient's choice, since we had found previously that otherwise the alcoholic, with his great capacity for rationalization, frequently stated that the results of various treatments were caused by "the liquor not being the right stuff". The beverages used varied in their alcoholic content, but the amounts consumed were the equivalent of 15–90 c.c. of absolute alcohol. Alcohol was given at varying times ranging from 1–36 hours after taking Temposil. No reactions were observed where alcohol was given more than 30 hours after the last dose of Temposil.

In Table I symptoms described by the patients are listed according to the time of onset.

TABLE I

Number of patients on 50 mg. Temposil	..	..	12
Number of patients on 100 mg. Temposil	..	..	36
Amount of alcohol equivalent of	..	..	15-90 c.c. absolute alcohol

Symptoms	No. of Patients Reacting on Dosage:		Average Time of Onset in Minutes	
	50 mg.	100 mg.	50 mg.	100 mg.
1. Feeling of well-being	8	8	12	4
2. Feeling of warmth	9	34	12	8
3. Headache	5	18	49	15
4. Tightness in chest	5	25	32	16
5. Pain in chest and arm	1	4	45	16
6. Palpitations	9	32	28	17
7. Increased desire to drink	8	11	10	20
8. Paraesthesiae	2	5	16	31
9. Nausea	1	6	90	41
10. Shivering	1	9	60	54
11. Apprehension	1	17	45	56
12. Dizziness	1	7	70	56

In 12 patients given alcohol after taking 50 mg. of Temposil typical acetaldehyde reactions were observed, but this was marked in only one case. The most striking feature of these tests was that eight patients expressed feelings of well-being with increased desire to drink. Further alcohol (in five cases to the equivalent of 90 c.c. of absolute alcohol) did not intensify the acetaldehyde reaction. This response has not been reported elsewhere although it is of considerable importance in the use of Temposil in long-term treatment of alcoholism. The effects of 100 mg. doses of Temposil were further studied to see whether this factor could be modified or eliminated.

The pattern of alcohol-Temposil reaction is fairly constant in development and a brief account on each symptom and its correlation with physical findings will be made.

A feeling of well-being was an early symptom, more prominent in the 50 mg. group. After taking alcohol eight (66 per cent.) of these cases became elated, jocular and expansive in manner, a feature which persisted despite later development of an acetaldehyde reaction. Eight patients (22 per cent.) treated with 100 mg. of Temposil expressed similar feelings of well-being but this was sustained in only four cases when the reaction became more marked.

A feeling of warmth was the most common finding and was closely connected with the observed signs of flushing, urticaria and conjunctival injection.

Headache was usually described as beginning with hot tight sensations of frontal distribution, gradually developing to a more generalized throbbing ache which persisted for periods lasting up to six hours. This was the most prolonged effect of alcohol-Temposil reaction and would appear to suggest that the cerebral vessels develop a greater degree of sensitivity to acetaldehyde after Temposil than is observed in other parts of the cardiovascular system.

Tightness in the chest and throat was usually described as "difficulty in breathing in", the patients being aware of having to "push" air into the lungs. When these symptoms were prominent bronchospasm was noted on auscultation.

Pain in the chest and arm was found in four cases. These patients had complained of palpitation and tightness in the chest to a greater degree than average

before feeling pain. Pain was of a cramping nature and affected the whole chest wall at first. With continued fall in blood pressure the pain usually became more localized over the praecordium before radiating down the left arm. In one case the pain radiated down both arms with cramp-like sensations in the fingers. Three cases had cardiac irregularity at the same time, but this was not marked.

Palpitation was closely related to increase in the pulse rate and volume and was most marked in severe reactions.

Increased desire to drink was found in eight cases (66 per cent.) in the 50 mg. group. Eleven (30 per cent.) treated with 100 mg. Temposil showed increased desire to drink but this was sustained in only four cases (11 per cent.) when other features of the reaction became more marked.

Paraesthesiae were described in seven cases and usually as widespread tingling sensations affecting all parts of the body, particularly the extremities. This symptom was noted in association with an increased desire to drink.

Nausea was an infrequent finding of late onset, found in only two cases.

Shivering and a feeling of coldness were of late onset and were found only in severe reactions.

Apprehension was expressed by 18 patients and was associated with severe degrees of tightness and pain in the chest, shivering and shock. This was not, however, a very serious symptom except in one case where the total reaction was atypical, occurring two hours after taking alcohol.

Dizziness was described as a sense of haziness with a feeling that the room was no longer fixed and steady. Of late onset this symptom usually disappeared when the patient lay flat on the bed. In assessing the severity of a reaction dizziness was of little value, being marked in six cases where the general reaction was slight or moderate.

In Table II the physical signs observed are summarized according to the systems affected, but they also fall into a consecutive time sequence.

TABLE II

Signs	No. of Patients Reacting on Dosage:		Average Time of Onset in Minutes	
	50 mg.	100 mg.	50 mg.	100 mg.
1. Flushing	12	36	13	5
2. Urticaria	6	26	28	12
3. Conjunctival injection ..	3	25	33	15
4. Bronchospasm	1	17	20	15
5. Increased respiratory rate ..	—	4	—	25
6. Increased pulse rate	12	36	25	19
7. Change in blood pressure ..	7	31	35	40
8. Shock	1	6	70	60
9. Cardiac irregularity	—	5	—	75
10. Perspiration	3	8	23	25
11. Drowsiness	1	5	140	44

Flushing affected mainly the face, neck and upper trunk, but was also seen in the limbs. This was usually the first reaction, but the degree of flushing did not provide any accurate indication of later severity of response. Urticarial rashes appeared after flushing as scattered patches of map-like erythema on the trunk, arms and legs. No patient complained of pruritus or other abnormal sensation in the areas of urticaria which faded before the flushing subsided.

Conjunctival injection with lachrymation occurred less often, but gave a good indication of the severity of the reaction, which could be expected. Marked

reddening of the conjunctivae with free flow of tears was invariably associated with severe reactions.

These signs appear to have been produced both by direct action of increased acetaldehyde concentration and also by alteration of the vascular reaction to acetaldehyde.

Respiratory signs were difficult to assess since although patients commonly complained of tightness in the chest and breathing sounded laboured only four patients showed a definite increase of respiratory rate. A more common finding was bronchospasm, presumably a true allergic response of the respiratory passages to acetaldehyde. Perspiration was not common except in severe reactions.

Drowsiness was an infrequent finding of late onset lasting from 15–30 minutes.

Increase in pulse rate was found in every reaction and varied from a rise of 30 per minute to as much as 70 per minute. In general the greater the increase in the pulse rate, the more severe the reaction, but in some cases palpitation and increases of pulse rate of 40–60 beats per minute were found in otherwise slight reactions.

Changes in blood pressure followed a common pattern with a slight increase in diastolic pressure of 10–15 mm. Hg about 15 minutes after alcohol. In those cases with feelings of well-being and increased desire to drink this increase in blood pressure was maintained during the whole reaction. In the other cases the initial rise was followed by a fall in the diastolic pressure of 20–30 mm. Hg. Very severe reactions were marked by falls in the diastolic pressure of 40–50 mm. Hg. In cases treated with 100 mg. Temposil who at first expressed feelings of well-being and increased desire to drink and then later lost these symptoms the change in attitude was closely related to fall in blood pressure.

A state of shock was seen in 7 cases occurring approximately one hour after taking alcohol. These patients had earlier complained of shiverings and feelings of cold. On examination they were pale and worried looking with clammy sweating, rapid pulse of poor volume and falls of 40–50 mm. Hg in diastolic pressure. Five cases also showed transient irregularity of cardiac rhythm. It seems probable that the state of shock was due not only to the sudden fall in blood pressure caused by widespread vasodilation, but perhaps also to a direct toxic effect of acetaldehyde on the myocardium.

In Table III the severity of the reactions is assessed.

TABLE III

Degree of Reaction							After 50 mg. "Temposil"	After 100 mg. "Temposil"
Severe	..	..	..	..	..	..	1	14
Moderate	..	..	..	..	..	..	3	16
Slight	..	..	..	..	..	..	8	6

In the reactions graded severe, palpitation, pain and tightness in the chest, bronchospasm and shock were prominent.

In 15 cases so graded, attempts were made to assess the value of anti-histamine therapy in modifying the reaction. The substance used was mepyzamine maleate (Anthisan) (N-dimethylaminoethyl-N-p-methoxy-benzyl-a-aminopyridine maleate) given intravenously in a dose of 0.05 g. In all cases there was a substantial reduction in the severity of the symptoms and signs causing distress within two to four minutes of giving the injection. Such

symptoms as palpitation, tightness and pain in the chest were rapidly eased with return of pulse rate and blood pressure to normal values. Patients who were apprehensive and worried about the outcome of the reaction became less anxious. Use of Anthisan did not appear to shorten the duration of flushing, urticaria or conjunctival injection and did little to modify headache. The efficacy of Anthisan in arresting symptoms confirms the view that part at least of the alcohol-Temposil reaction is an allergic phenomenon

Acetaldehyde reactions not interrupted lasted from $1\frac{1}{2}$ to 3 hours with an average duration of two hours. Apart from continued headache the other observed symptoms and signs had settled in this period.

One case, a man aged 49, treated with 100 mg. of Temposil and the equivalent of 30 c.c. of absolute alcohol merits a short comment.

This patient had had a partial gastrectomy four years previously; following ingestion of alcohol he developed a moderate reaction after ten to fifteen minutes. Two hours later he suddenly showed a sharp drop in pulse rate from 120 to 40 per minute with a coincident fall in blood pressure from 140/90 to 70/50. He was profoundly shocked and began to vomit. Anthisan (4 c.c.) was given intravenously with little effect, but after intravenous injection of mephine (15 mg. mephentermine sulphate in 1 c.c.) blood pressure and pulse rate returned to normal values. This very delayed reaction was presumably due to the relatively rapid passage of the alcohol through the small remaining part of the stomach with subsequent slow absorption of alcohol from the small intestine and, therefore, delayed production of acetaldehyde.

In ten cases given alcohol 36 hours or more after the last dose of Temposil no acetaldehyde reaction was found. In a further 7 cases who had indulged in alcohol while on maintenance treatment it appeared from the patient's comments that they had found themselves able to drink without symptoms within 24-36 hours of the last dose of Temposil. This confirms the observation of other workers that Temposil is excreted within 24 to 36 hours (1, 5, 14).

Of the 33 patients who were given test reactions only 27 were regarded as suitable for continued treatment. Five who had shown markedly increased desire to drink after small quantities of alcohol and minimal acetaldehyde reaction were omitted. The sixth patient was an alcoholic paranoid schizophrenic who refused to take the drug.

In Table IV the results of treatment to date are briefly summarized:

TABLE IV

Time on "Temposil" in Months				No. of Patients	No. Abstinent	No. Relapsed
Less than 1 month	..	..	..	10	6	4
1-3 months	..	..	..	9	6	3
3-6 months	..	..	..	4	3	1
6-12 months	..	..	..	3	3	—
Over 12 months	..	..	..	1	1	—
Total	..	..	..	27	19	8

It would appear from the limited series we have investigated that there is a high correlation between duration of use of Temposil and abstinence from alcohol. Those patients who take the drug for periods of less than three months have considerably higher relapse rates than those who have used it for longer periods. Periods of abstinence so far range from 2 months to 15 months.

No serious side-effects of prolonged usage have been noted. Regular blood counts, urinalysis and liver function tests have been done in the majority of cases treated and no abnormalities have been detected. Two patients have complained of transient epigastric discomfort for short periods after taking the tablets. One patient had an exacerbation of longstanding acne vulgaris which settled when the dose of Temposil was reduced from 100 mg. to 50 mg. No other side-effects have been observed.

DISCUSSION

Temposil does not produce unpleasant side-effects such as those found with disulfiram. There is, therefore, less difficulty in persuading patients to take the drug regularly.

If alcohol is taken within 24 hours of taking Temposil an acetaldehyde reaction is produced within 15 minutes. All cases in this series showed some degree of acetaldehyde reaction, whereas alcohol-disulfiram reactions are much less predictable probably due to storage of disulfiram in body fat depots (3).

Alcohol-Temposil reactions are not so severe as those found with disulfiram. The severity of the reaction can rapidly be minimized by intravenous injection of an anti-histamine, whereas disulfiram reactions are not easily modified.

In six cases who took alcohol within 24 hours of taking Temposil the interesting observation was made that when reactions developed the patients were able to reduce the intensity of the symptoms by walking about briskly. One of us (A.M.) during a test reaction not included in the above results confirmed these patients' reports that symptoms appear less prominent when an effort was made to keep walking as quickly as possible.

Only one case in this series would have been unable to walk about because of the severity of the reaction. Temposil would seem, therefore, to be a safer drug in the treatment of alcoholism than disulfiram.

The main disadvantage would appear to derive from the occurrence of increased desire to drink in the early stages of alcohol-Temposil reactions, but this difficulty can be overcome by conducting individual test reactions under close observation before beginning long-term use. It is essential to carry out these test reactions, as otherwise the alcoholic may have additional problems arising from treatment ostensibly aimed at helping him.

The above findings suggest that 100 mg. Temposil provide a more suitable dose than 50 mg. suggested by other workers.

SUMMARY

1. The composition and mode of action of Temposil are described.
2. An analysis of 48 alcohol-Temposil reactions is made.
3. A method of modifying alcohol-Temposil reaction using anti-histaminic drugs is described.
4. Results of prolonged use in 27 patients are described.
5. Some comments are made regarding the value of Temposil in comparison with disulfiram.

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STEROID EXCRETION IN RELATION TO WEIGHT IN MENTALLY DEFECTIVE BOYS

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COHEN (1958) has shown that obese children have increased 17-ketogenic steroid excretion and Norval and King (1950) showed that urinary corticosteroids in normal children were closely related to their weight. Lugg and Bowness (1957) found a positive correlation between weight and 17-ketosteroid excretion in adults. Dutton (1958) found that mongol boys were about 15 per cent. over weight for their height although their height and weight were depressed for their life age.

It seemed therefore that an investigation into the steroidal status of mongol boys was indicated which compared the excretion of 17-keto and ketogenic steroids in relation to weight and not to age. The comparison of the mongol boys with other non-mongol mental defective boys in the same environment and in the same age group seemed to be a worthwhile study.

THE MATERIAL

The diagnosis of mongolism was on clinical grounds and no doubtful cases have been included in this survey. Twenty-four hour specimens from 29 mongol boys aged between 7 and 16 years were examined.

The control group was taken from a group of non-mongol mental defective boys of the same age group; this group is necessarily a very heterogeneous collection but they lived in the same environment as the mongols. The control group was 50 in number and 24-hour specimens of urine were examined in parallel with the specimens obtained from the mongols.

THE METHODS

The 24-hour specimens were collected without added preservative but the analysis was started within 3 hours of the termination of the collection.

17-Ketosteroids. These were estimated by the modified method of Callow *et al.* (1938) and Robbie *et al.* (1943) given in Delory (1949) with the colour correction of Talbot *et al.* (1942).

17-Ketogenic Steroids. These were estimated by the Sodium Bismuthate method of Norymberski *et al.* (1953) with the modification quoted by Moxham and Nabarro (1956).

Weight. This was measured naked, apart from a pair of thin underpants, on a beam type of balance, weighing being to the nearest $\frac{1}{2}$ pound.

THE RESULTS

Table I shows the mean 17-keto and ketogenic steroid excretion, in mg. per day, in the two groups of mental defective boys by 10 pound weight increments. Figures 1 and 2 show the same results expressed graphically.

TABLE I

Mean Daily Excretion of 17-keto and 17-ketogenic Steroids in mg. in Two Groups of Mentally Defective Boys Compared with Body Weight in Pounds

Weight Group	Number		Mean 17-keto-steroids		Mean 17-ketogenic Steroids	
	Mongols	Non-Mongols	Mongols	Non-Mongols	Mongols	Non-Mongols
40- 50 ..	4	10	0.7	1.6	1.5	3.5
50- 60 ..	4	5	2.5	2.2	3.8	3.3
60- 70 ..	8	9	2.4	2.2	5.3	5.5
70- 80 ..	8	8	2.5	2.7	6.8	6.0
80- 90 ..	2	2	5.7	2.9	3.3	7.8
90-100 ..	2	5	9.1	4.7	9.8	8.4
100-110 ..	1	4	10.5	4.8	9.9	12.8
110-120 ..		1		3.5		5.5
120-130 ..		3		5.7		10.2
130-140 ..		1		3.0		10.8
140-150 ..		2		6.5		13.7

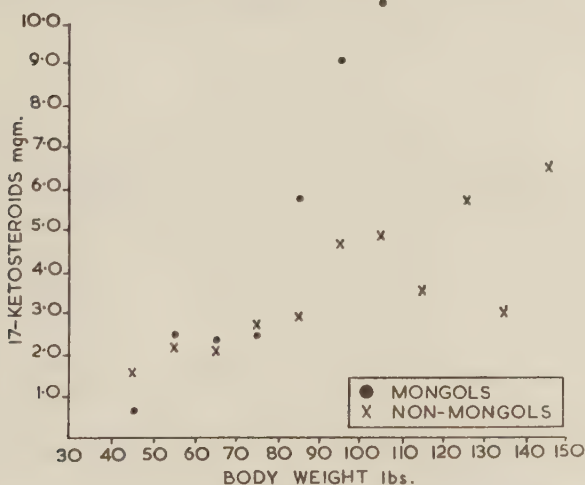


FIG. 1.—To show mean 17-ketosteroid excretion per day compared with mean body weight in 2 groups of mentally defective boys.

Table II gives a statistical analysis of the raw figures and shows a high degree of correlation between the steroid excretion and weight for the 17-ketosteroids in mongols and both steroids in the non-mongol group. In the mongols "r" is significant at the 5 per cent. level at 0.381 and the coefficient correlation ratio for the mongols is for 17-ketosteroids +0.715 and for the 17-ketogenic steroids +0.353, the latter being non-significant. In the non-mongol group the significant level of "r" is 0.280 and the coefficients of correlation are for 17-ketosteroids +0.688 and for the 17-ketogenic steroids +0.582; both these

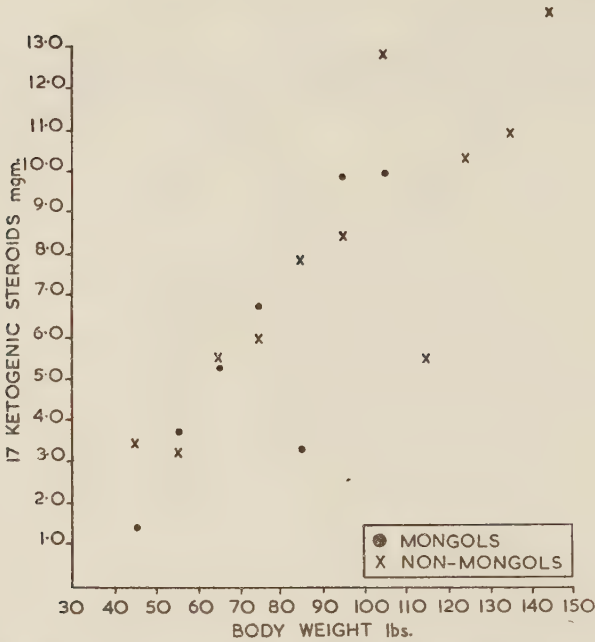


FIG. 2.—To show mean daily excretion of 17-ketogenic steroids compared with body weight in 2 groups of mentally defective boys.

TABLE II

To Show the Correlation Between 17-ketosteroid and 17-ketogenic Steroid Excretion and Body Weight in Two Groups of Mental Defective Boys

Group	No.	Coefficient of Correlation "r"		Significance
		17-ks./wt.	17-kgs./wt.	
Mongols	29	+0.715	+0.353	"r"=0.381 significant at 5% level
Non-mongols	50	+0.688	+0.582	"r"=0.280 significant at 5% level

figures show there to be a significant correlation between ketosteroid excretion and weight.

It has been possible to calculate from the raw figures linear regression equations for the 17-ketosteroid excretion against weight in the two groups of children. Since the correlation between 17-ketogenic steroids and weight was not significant in mongols it is not worth while to pursue this line of analysis.

The equations of linear regression in the two groups are:

Mongols: 17-ks=0.14 (body weight pounds -68) +3.1

Non-mongols: 17-ks=0.049 (body weight pounds -76.7) +3.06

17KS=Daily excretion of 17-ketosteroids in mg.

Figure 3 shows the two regression lines for 17-ketosteroid excretion against weight in the mongol and non-mongol boys. It will be seen that there

is a marked difference between the two groups and this difference is not accounted for by differences in weight alone for Figure 4 shows the mean weights for each year of age in the two groups.

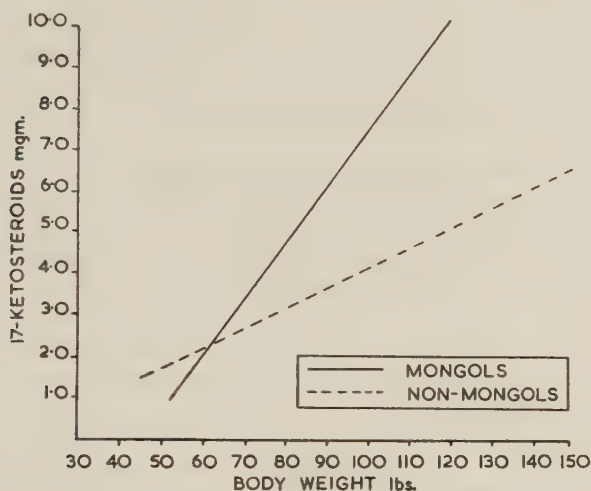


FIG. 3.—To show linear regression of 17-ketosteroids on weight in 2 groups of mentally defective boys.

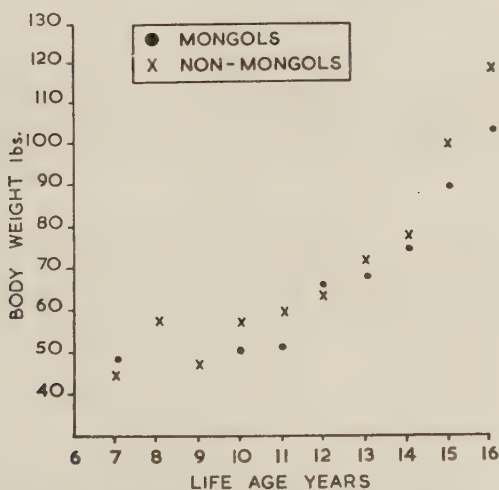


FIG. 4.—To show mean body weight for age in 2 groups of mentally defective boys.

DISCUSSION

Borth *et al.* (1957) in a study of urinary 17-hydroxycorticosteroid and 17-ketosteroid excretion showed a correlation with age, height and body weight but the two steroid fractions differed in their degree of correlation. The dependence on age was more pronounced and the joint effect of body weight and height smaller for 17-ketosteroids than 17-hydroxycorticosteroids and for the latter the sex difference in excretion levels could be accounted for solely by the

difference in body size whereas men could be expected to excrete about 30 per cent. more 17-ketosteroids than women of the same age and build.

Gray *et al.* (1956) found no significant difference between adipose and normal children in the excretion of 17-ketosteroids but the comparison was on age alone and weight was not taken into consideration.

When mongol and non-mongol boys are compared on an age basis alone there is no significant difference between the levels of excretion of 17-ketosteroids and 17-ketogenic steroids in the two groups (Dutton, 1959a) nor is there demonstrable difference between the mentally defective boys and normal children.

There is substantial evidence that under-nutrition leads to functional hypopituitarism (Talbot *et al.*, 1952; Perloff *et al.*, 1954) and it has been suggested by Cohen (1958) that the converse may be true. In mongols, however, although they are over weight for height (but not for age) there is no evidence of hyperpituitarism, in fact the converse is more likely since the failure in linear growth may well be due to a lack of growth hormone (Dutton, 1959b). The sexual maturation of mongols starts at the normal time as compared with other mental defectives and with the norms in the literature but often they do not develop full sexual maturity.

One can only conclude therefore, that the mongol has a relative increase in 17-ketosteroid excretion when weight is taken into consideration as compared with the non-mongol mental defective boy. This increase would seem to be due to a primary testicular effect since the 17-ketogenic steroid excretion level does not suggest hyperadrenalism and the somatic growth of mongols is such as to suggest that there is pituitary lack rather than excess.

SUMMARY

The results of steroid analysis in 2 groups of mental defective boys is given, comparison being on a weight basis. It is suggested that the discrepancy between the groups is due to a difference in testicular function.

ACKNOWLEDGMENTS

My thanks are due to Dr. J. M. Crawford, Physician Superintendent at Botleys Park Hospital, Chertsey, for permission to undertake this survey; to Mr. P. Purkiss, the laboratory technician at Botleys Park, for his help in the steroid assays and to the nursing staff and patients for their help in providing the necessary specimens.

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CLINICAL STUDIES WITH LSD-25 AND TWO SUBSTANCES RELATED TO SEROTONIN*

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PART I

CLINICAL REACTIONS OF NORMAL HUMAN SUBJECTS GIVEN LSD-25 AND AN
ANTI-METABOLITE OF SEROTONIN (1 BENZYL-2, 5-DIMETHYLSEOTONIN HYDRO-
CHLORIDE) (BAS)

INTRODUCTION

IN 1953, Twarog and Page (1) demonstrated that 5-hydroxytryptamine (serotonin) is present in relatively high concentrations in the brain. At about the same time Gaddum (2) and Woolley and Shaw (3) observed that LSD is a highly potent serotonin antagonist in such tissues as rat uterus and hypothesized that the hallucinogenic effect of LSD might be due to interference in the action of serotonin.

Following these discoveries, several workers attempted to test this hypothesis on a clinical level in humans. Montanari and Tonini (4) reported the successful use of intramuscular serotonin as an antagonist to the psychological effects of LSD-25 in humans. In contrast to these findings, Sjoerdsma, Kornetsky and Evarts (5) reported the administration of LSD-25 in two patients who suffered from malignant carcinoid. Both patients experienced all the usual effects of LSD-25.

There is an obvious contradiction between the two latter reports. The validity of the study by Montanari is open to question, however, since serotonin is rapidly destroyed by amine oxidases in the blood (6), and if injected, probably would not reach the brain in effective concentrations. Furthermore, serotonin does not cross the blood brain barrier in appreciable amounts. In the carcinoid patients, on the other hand, a large, continuous output of serotonin obviates the first objection, but the blood brain barrier problem remains.

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Chemical determinations were done by Margaret Filbert, M.S.

Gaddum (7) has tested this hypothesis himself in cats. Serotonin was injected directly into the cerebral ventricles. This was followed by LSD administration. The LSD reactions did not appear to be significantly affected by the serotonin. This result is highly significant, and casts considerable doubt on the basic hypothesis; yet observations of psychological changes in animals are necessarily crude, and allow little scope for noting subtle changes. Thus, in spite of these important findings, it would seem desirable to carry out further clinical studies in humans.

Gaddum originally advanced his hypothesis after it had been observed that LSD and serotonin are antagonists *in vitro*, on such tissues as rat uterus. More recently it has been demonstrated by Delay and Thuillier (8) that this antagonism exists only with relatively high concentrations of LSD. When LSD concentrations are lower, at levels corresponding to those exerting psychotic effects in man, it potentiates the effects of serotonin on rat uterus. Woolley and Shaw (9) have also reported that LSD has effects similar to those of serotonin on tissues such as oligodendroglia from the brain, and on the heart beat of the clam, *Venus mercenaria*.

With these findings in view, if we are to make inferences about the relationship between serotonin and LSD in mental functioning it would seem possible that LSD acts by potentiating the effects of serotonin normally found in the brain. If this should be true, then a specific antagonist towards serotonin would be expected to block the psychological effects of LSD.

Woolley and Shaw (10) have reported on an orally active benzyl analogue of serotonin (1-benzyl-2, 5-dimethylserotonin hydrochloride) referred to as BAS. This substance acts as an anti-metabolite to serotonin. Presumably it is bound by the same substrate as serotonin, thereby preventing serotonin from acting. Wilkins (12) reported the use of this substance in hypertensive medical patients, in whom it causes moderate lowering of blood pressure. Side-effects include sedation or sleepiness, some slowing of the pulse, mild nasal stuffiness and abdominal cramps. In these studies, doses of 40 to 160 mg. a day were used.

In view of these considerations, the authors considered it worth while to test BAS as a potential antagonist to the psychological effects of LSD. Since our studies were concluded, other studies reporting the clinical use of BAS have been reported (13, 14). Since the work described in this paper was completed (in 1957), a paper by Isbell, *et al.* (20) has appeared in which a similar experiment using BAS with LSD-25 is reported. Isbell also found the BAS to have no influence on the LSD reactions.

PROCEDURE

In the pilot studies, BAS was given in divided doses—the first dose of 100 to 200 mg. was given on the night preceding the experiment, and the second dose approximately $\frac{1}{2}$ to 1 hour before LSD administration. BAS was not found to exert any effect on the LSD reaction.

After pilot studies,* using eight subjects, the following study was performed. Six "normal" male volunteers were selected for the study. One of three drug

* Tables II and III show the independent ratings of both observers in terms of relative severity of the reactions. Drugs were all administered on a double-blind basis. Both raters correspond with one another and with the schedule of administration, only in Column 3. In Columns 1 and 2 the observer's ratings are only in 50 per cent. agreement, which is no better than chance. It will also be seen that observers' ratings in Columns 1 and 2 correspond no better with Table I than with each other.

The authors conclude from this that the BAS administered produced no consistent effect in either direction on the severity of the LSD reactions.

combinations was administered to each subject, on each of three experimental days, one week apart. Each subject received all three drug combinations on separate days.

The design employed is shown in Table I.

TABLE I

Table Shows that on Any Experimental Day there were Two Subjects Receiving Each Drug Combination

	Day			Drugs		
				Column 1 LSD + Placebo	Column 2 LSD + BAS	Column 3 BAS + Placebo
1	..	..	..	A, B	C, D	E, F
2	..	..	..	D, F	B, E	A, C
3	..	..	..	C, E	A, F	B, D

Subjects labelled A, B, C, D, E, F.

TABLE II

Ratings of Rater 1 (GDK)

	Day			Column 1	Column 2	Column 3
				Most Severe	Medium Severe	Least Severe or None
1	..	..	..	A, D	B, C	E, F
2	..	..	..	B, E	D, F	A, C
3	..	..	..	C, F	A, E	B, D

TABLE III

Ratings of Rater 2 (EC)

	Day			Column 1	Column 2	Column 3
				Most Severe Reaction	Medium Severe Reaction	Least Severe Reaction or None
1	..	..	..	B, D	A, C	E, F
2	..	..	..	E, F	B, D	A, C
3	..	..	..	A, C	E, F	B, D

LSD was administered orally in doses of 100 micrograms dissolved in distilled water. BAS was given orally in two doses. Two hundred milligrams was given one-half hour before LSD, and another 100 mg. was given one-half hour following LSD administration. Double-blind procedure was followed.

Each subject was rated three to five times on each experimental day by each of two psychiatric observers, working independently, and all were interviewed on the following day. Ratings were recorded on a rating sheet which allows for quantitative and qualitative ratings of physiological and psychological changes. Both objective and subjective factors were considered.

This method of rating has been used with considerable success by the authors in another study (15). We have found that where differences in relative severity of response exist, they can be reliably detected.

With the design which was followed, it was possible to compare subjects against one another, and each subject against himself with regard to severity of reactions on the various experimental days.

If BAS acted as an antagonist to LSD, then we should have expected subjects receiving combinations of LSD and BAS to be rated as having milder

reactions than those receiving only LSD. If, by any chance, BAS potentiated the action of LSD, then we should expect the LSD-BAS subjects to have the more severe reactions. Administration of BAS by itself gave us a chance to see what effects, if any, this drug had on psychological functioning.

The effects of more prolonged premedication of BAS upon the LSD reaction was studied in two subjects. Each was given BAS, 100 mg. q.i.d., for three successive days. On the fourth day each received 200 mg. BAS, followed by 1 microgram per kg. of LSD-25. Each subject received 1 mcg./kg. LSD on another occasion, without BAS, for comparison.

RESULTS

Both raters were 100 per cent. successful in distinguishing the 6 BAS-placebo responses from the others, as would be expected: neither rater succeeded in distinguishing the LSD-BAS reactions from the LSD-placebo reactions with any greater degree of accuracy than might be expected from chance. Nor did the raters agree any better with one another in this (see Tables II and III). In the smaller study, in which two subjects were given more prolonged dosage of BAS, the BAS produced slight drowsiness, but no effect on the severity of the LSD reaction was observed, subjectively or objectively.

DISCUSSION

Since, in other studies, we have been able to accurately rate the relative severity of LSD reactions, it appears rather clear that BAS had no significant effect on the reactions of these subjects to LSD.

The physiological significance of this finding is not yet clear, unfortunately, since it is not known with certainty whether BAS crosses the blood brain barrier. The symptoms of drowsiness from BAS reported by our subjects and by Wilkins's patients strongly suggest that it does, but this is not conclusive evidence. Further evidence, however, has come recently from Rudy, *et al.* (16) and from Rinaldi (17). The former author has reported a tranquilizing action of BAS, resembling reserpine effects in chronic schizophrenic patients, while Rinaldi has shown that BAS causes EEG changes in rabbits when administered intravenously, and in some humans (three out of fifteen) when administered orally.

There is also some evidence to the contrary. Woolley and Shaw (18) have shown that BAS injected peripherally in mice produces no behavioural effects. When injected into the brain of the animal, however, it causes distinct behavioural changes. This suggests that BAS does not normally cross the blood brain barrier, but that it is active when introduced directly into the brain, at least in mice.

Gaddum (19) himself, has already observed that BOL (2-Brom-LSD) and a variety of other substances which antagonize serotonin lack its potency as a psychotomimetic agent. Gaddum further indicates that these observations "diminish the value of the existing evidence favouring this theory" (i.e. that LSD acts by influencing serotonin action in the brain).

If we assume that BAS does cross the blood brain barrier in effective concentrations, our results cast further doubt on the theory.

SUMMARY

A study was carried out to test whether an anti-serotonin in the form of a chemical analogue of serotonin (1 benzyl-2, 5-dimethylserotonin hydrochloride),

referred to as BAS, would antagonize the psychological effects of LSD-25. A modified Latin Square design was followed, in which 6 normal subjects each received LSD+placebo; LSD+BAS; and BAS+placebo on three separate experimental days. Double-blind procedure was followed. In a smaller study two subjects were given LSD-25 following more prolonged premedication with BAS. Subjects were rated for relative severity of response with each of the drug combinations. LSD-BAS responses were not significantly different from LSD-placebo responses. Though there are conflicting reports regarding the question of whether BAS crosses the blood brain barrier, recent evidence suggests that it does. If we assume that this is true, these results cast doubt on the hypothesis that LSD-25 acts by affecting serotonin action in the brain.

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PART II

CLINICAL REACTIONS OF NORMAL HUMAN SUBJECTS GIVEN 5-HYDROXYTRYPTOPHAN (A SEROTONIN PRECURSOR) AND LSD-25

Udenfriend *et al.* (1) have reported a method of significantly increasing brain levels of serotonin (5-hydroxytryptamine, 5-HT), in animals by administration of 5-hydroxytryptophan (5-HTP), a serotonin precursor. This compound is decarboxylated in the brain to form serotonin. Serotonin itself penetrates the blood brain barrier to only a slight degree. Udenfriend has also reported that 5-HTP produces effects in animals resembling the effects of LSD-25 (2). Davidson *et al.* (3) has demonstrated that in man also, 5-HTP is converted to serotonin, by recovering increased amounts of serotonin and 5-hydroxyindole-acetic acid (5-HIAA) in the urine after parenteral administration of 5-HTP: (5-HTP→5-HT→5-HIAA). 5-HTP was administered to 11 subjects by this author. In 10 subjects, a dose of 50 mg. or less was the maximum which could be given because of gastro-intestinal side-effects. In one subject a dose of 120 mg. was reached. No central nervous system effects were reported. They concluded that this dose of 5-HTP was inadequate for increasing brain serotonin to levels at which mental changes might be expected.

Bessman *et al.* (4) reported on the electroencephalographic effects of 10 mg. of intravenous 5-HTP in patients who were in hepatic coma. Slow activity was modified in the direction of a more normal pattern. 5-HIAA was found in the urine. This study offers further evidence that 5-HTP enters the brain, is converted to serotonin, and that neurophysiological effects can be produced. It suggests further, that serotonin has a role in normal brain functioning. It is of interest that a dose of only 10 mg. was effective in these patients.

As noted in Part I there has been much speculation regarding the inter-relationship between serotonin, and LSD-25 in the brain. The present study was designed with two purposes. The first was to test the hypothesis that LSD effects in the brain are related to some type of interaction with serotonin (5). The second purpose was to discern whether relatively large doses of 5-HTP produce any psychological effects in normal subjects.

METHOD

A pilot experiment was undertaken to study possible interaction between LSD-25 and 5-HTP. Two volunteers were administered 50 mcg. of LSD-25 orally and 50 mg. of 5-HTP intravenously at weekly intervals as follows: one week 5-HTP followed by LSD-25, 15 minutes after the 5-HTP infusion was completed; and one week LSD-25 followed by 5-HTP 60 minutes later; and one week LSD-25 alone.

Following this a more controlled study was undertaken, employing four subjects and a double-blind procedure. (The double-blind was not entirely successful, however, since 5-HTP could usually be identified by the G.I. symptoms it produced.) The dose of LSD-25 administered orally, was decreased to 30 mcg. since with this amount, effects are usually just perceptible. Consequently any enhancement of LSD-25 effects by 5-HTP could be more readily discerned. The dose of 5-HTP was increased to 150 mg., administered by slow intravenous drip. (One subject received only 120 mg. because of persistent nausea and vomiting.) LSD was given following completion of the infusion. The subjects were not informed as to what drugs were to be used, but were told that their behaviour might be affected by either of the drugs. Each volunteer received placebo (i.v. saline) plus LSD-25 one week, and 5-HTP plus LSD-25 the following week. Urinary serotonin and 5-HIAA were determined for two consecutive four-hour periods beginning at the start of the i.v. infusions (Table I).

TABLE I

Urinary Excretion of 5-HIAA and Serotonin Following 5-HTP or Saline Administration
(Subjects received LSD-25 in combination with 5-HTP or saline on each occasion)

Subject	Date	Drug	Dose	Urinary Serotonin*		Urinary 5-HIAA*	
				1st Period	2nd Period	1st Period	2nd Period
A	.. 11/3/58	5-HTP	120 mg.	↑	↑	↑	↑
	18/3/58	Saline	200 cc.	Norm	Norm	Norm	Norm
B	.. 11/3/58	Saline	200 cc.	Norm	Norm	Norm	Norm
	18/3/58	5-HTP	150 mg.	↑	↑	↑	↑
C	.. 11/3/58	Saline	200 cc.	Norm	Norm	Norm	Norm
	18/3/58	5-HTP	150 mg.	↑	—	↑	—
D	.. 11/3/58	5-HTP	150 mg.	↑	↑	↑	↑
	18/3/58	Saline	200 cc.	Norm	Norm	Norm	Norm

* Although quantitative determinations of urinary serotonin and 5-HIAA were done, the results are not listed quantitatively because of technical difficulties which led to minor inaccuracies in the results.

After completion of these studies, one of the four subjects who appeared to have a psychological reaction to 5-HTP was administered a larger dose (200 mg.) of 5-HTP intravenously, and observed clinically (see Results).

RESULTS

All four subjects in the controlled study had a significant rise of both serotonin and 5-HIAA excretion after 5-HTP administration. No G.I. effects from 5-HTP were reported by either of the subjects used in the pilot study. Among the other four subjects, two vomited and a third experienced nausea. Regarding the effects of 5-HTP on the LSD reactions; both subjects in the pilot study reported that the LSD reaction was slightly stronger when 5-HTP was given. The experimenters could see no significant difference, however. Among the other four subjects, two reported slightly stronger LSD reactions from the LSD-5-HTP combination, while the other two reported slightly more severe reactions from LSD-placebo. The experimenters could not distinguish between the LSD-5-HTP and LSD-placebo combinations except by the nausea produced by 5-HTP.

One volunteer (C) during placebo i.v. (before LSD administration) noted some difficulty in concentration (reading, Serial 7 subtraction), felt "woozy", and had twitching of his left index finger. These effects lasted approximately 45 minutes. Another subject reported mental effects during 5-HTP administration. These consisted of restlessness, difficulty in concentrating, and a mild feeling of timelessness.

As mentioned above, the volunteer who had mental effects following the 5-HTP infusion was again administered 5-HTP intravenously. Nausea was reported early after the start of the experiment, but this was controlled by slowing the rate of the infusion. After 180 minutes, a total dose of 200 mg. of 5-HTP was administered. The infusion was stopped because of persistent nausea and imminent vomiting. The subject again noted "dizziness", restlessness, impairment of concentration and in addition reported "after images". These changes were entirely subjective. Within one hour after the infusion was completed all psychological symptoms had abated, and did not recur. A blood pressure increase was observed fifteen minutes after the termination of the intravenous drip. The highest blood pressure recorded was 170/110 at this time, gradually decreasing to control levels (130/80) three hours later. No electrocardiographic abnormalities occurred.

DISCUSSION

Because of the limited number of subjects included in the study only tentative conclusions can be reached. The results indicate, however that 5-HTP has little or no effect on the qualitative or quantitative aspects of the LSD reaction, at least in the doses employed. As noted above, it has been shown that 5-HTP is converted to serotonin in the brain. In view of this, these results further weaken the hypothesis that LSD produces its psychological effects via some type of interaction with serotonin or its receptors in the brain.

The one subject who reported subjective psychological effects from 5-HTP alone is worthy of comment. We have observed several other subjects who were not included in this study who also reported mild, transient effects of the same sort from 5-HTP, but not from placebo controls. Since such effects are sporadic—subjective and fleeting—it is difficult to determine whether or not one is dealing with a "will-o-the-wisp" or some genuine effects of the drug. (It will

be noted that one subject reported similar effects from the saline control.) The question probably could be answered, if larger doses of 5-HTP could be given. This might be accomplished if a substance were found which would block the peripheral, but not the central effects of 5-HTP and/or serotonin. For the time being, the matter is open to conjecture.

SUMMARY

Six subjects (2 in a pilot study and 4 in a later study) were given doses of LSD-25 in combination with 5-hydroxytryptophan (5-HTP), a serotonin precursor, which raises brain serotonin levels. Saline placebo was also administered on separate occasions as a control for the effects of 5-HTP. Urine samples were collected for determinations of serotonin and 5-hydroxy-indoleacetic acid (5-HIAA). The chief purpose of the study was to test the hypothesis that 5-HTP by increasing brain serotonin levels would alter the severity of the LSD reactions. Secondarily, the authors were interested in observing any possible psychological effects of 5-HTP itself.

The results were as follows:

1. Serotonin and 5-HIAA levels in the urine increased in each case following 5-HTP.
2. 5-HTP was not observed to produce any definite or consistent effects on LSD reactions.
3. One subject reported vague psychological effects from saline placebo, and another reported mild psychological effects from 5-HTP.

The need is indicated for further studies to elucidate the possible psychological effects of 5-HTP.

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THE EFFECTS OF 5-HYDROXYTRYPTOPHAN (A SEROTONIN PRECURSOR) IN SCHIZOPHRENIC PATIENTS*

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INTRODUCTION

WOOLLEY has repeatedly drawn attention to the possible role of serotonin (5-hydroxytryptamine) in mental functioning (1, 2, 3, 4). In particular, this author has stressed the possibility that some forms of mental illness, such as schizophrenia, may be related to disorders in cerebral serotonin metabolism.

The major experimental evidence in support of Woolley's arguments is as follows: (a) Serotonin is found in relatively high concentrations in certain parts of the brain (5, 6). (b) *In vitro*, serotonin and LSD-25, a psychotomimetic agent, act as antagonists or synergists, depending upon the concentrations of each, on such tissues as rat uterus and oligodendroglia (7, 8, 9, 10). (c) Langfitt, Hart and Marrazzi (11) have shown that serotonin inhibits transcallosal synaptic transmission as do mescaline, LSD-25, and amphetamine. (d) Abnormal behaviour has been reported to be induced in animals by elevated levels of brain serotonin (12), as well as by administration of an antimetabolite of serotonin (13).

Although the above experimental findings are highly interesting, most would agree that they provide a rather slim basis for hypothesizing about mental illness. Indeed, most of this evidence is misleading. For example, although LSD-25 and serotonin act as antagonists or synergists on certain tissues *in vitro*, it is doubtful that the psychotomimetic effects of LSD-25 are related to serotonin (14, 15). Furthermore, since LSD-25 does not typically produce psychological effects corresponding to those of mental illness of endogenous origin, one may legitimately wonder about the relevance of LSD to the question.

Despite these limitations, however, the question is a most intriguing one, and it seems surprising that so little has been done to test it clinically.

A logical approach to determining the psychological effects of serotonin

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in humans is to produce elevated brain serotonin levels and observe clinically and by psychological testing any effects which may occur. Since serotonin crosses the blood brain barrier very poorly (16) brain serotonin levels cannot be raised by parenteral administration of serotonin itself. Udenfriend (17), however, has reported a method of increasing brain serotonin levels in animals by administering a serotonin precursor, 5-hydroxytryptophan (5-HTP). This substance crosses the blood brain barrier and is decarboxylated in the brain to serotonin.

Since Udenfriend's report, the authors are aware of only one published study (18), in which 5-HTP was given to humans by Davidson *et al.** In this study 5-HTP was administered intravenously to 11 normal volunteers. The doses given were 50 mg. or less in all but one subject who received 120 mg. No psychological effects were reported by any of the subjects.

The present authors, in administering 5-HTP to normal subjects in doses of up to 200 mg. observed some occasional, transient psychological effects such as impaired concentration and a feeling of timelessness (19). Although these symptoms were difficult to attribute to the drug with certainty they were sufficiently interesting to suggest further studies.

Thus, we decided to administer 5-HTP to schizophrenic patients. Because of its apparent effect on some of our normals we hypothesized that if 5-HTP were to have any psychological effects in schizophrenics it would increase their symptoms rather than lessening them. For this reason schizophrenic patients who had recently gone into remission were chosen for study. In such patients an increase in symptoms could be more readily observed. Another advantage in using patients in remission for the study was that they would be better able to understand and co-operate in the experiment.

METHOD

Five female patients were selected for the study from the Perry Point VA Hospital. All were in relative remission. The age range was from 31 to 39 years. Four had been diagnosed as suffering from schizophrenic reactions, and one was diagnosed "depressive reaction" (Table I). Three of the five patients were registered nurses. The patient diagnosed as a "depressive reaction" was a woman with depressive mood and ideation, who had not been overtly psychotic. In addition to these symptoms, however, this patient manifested some degree of thought disorder suggestive of schizophrenia.

Each patient was approached individually by one of the experimenters several days before participating in the experiment. The nature of the study was explained in some detail, and the patient was told she could drop out of the study any time she chose. She was told that she would be given something by vein, and that it might be a drug or might be just water. If she noted any effects, either physical or mental, they were to be reported at once to the experimenter. Although all of the patients had some degree of anxiety regarding

* Since this article was submitted for publication, Feldstein, *et al.* (30) have reported the administration of 5-HTP to chronic schizophrenic patients in combination with 1 benzyl-2, 5-dimethylserotonin hydrochloride (BAS) and mersilid. It has also come to our attention that Woolley has reported the administration of 5-HTP and BAS in combination, to schizophrenic patients (31). In both cases the purpose was to determine any potential therapeutic value of 5-HTP. This, of course, is the exact opposite of the hypothesis we were testing. The results reported by these authors were all negative. We consider it unfortunate that BAS was given in combination with 5-HTP in these studies. It is highly probable that BAS crosses the blood brain barrier, and it may conceivably block the central effects of serotonin. In view of this possibility the results of these studies are difficult to interpret.

TABLE I

Subject	Age	Diagnosis*	Dose 5-HTP (mg.)
A	34	Schizophrenic reaction paranoid	100
B	39	Schizophrenic reaction acute undifferentiated ..	80
C	35	Schizophrenic reaction chronic undifferentiated	100
D	31	Schizophrenic reaction acute undifferentiated ..	100
E	39	Depressive reaction	100

* All patients were in a state of relative remission.

the procedures, most of them were quite interested and relatively enthusiastic. An effort was made to use them as scientific collaborators rather than merely as subjects.

Each patient was administered placebo (isotonic saline) on one experimental day and 5-HTP on another. Three patients received 5-HTP on their first day, and placebo on the second (at least one week later) while the order was reversed for the other two. Double-blind procedure was followed, although the observers could usually tell when 5-HTP was given because of the nausea and sometimes vomiting which were produced.

TABLE II

Subject						Week 1	Week 2
A	..	..	..	..	..	5-HTP	Placebo
B	..	..	..	..	..	Placebo	5-HTP
C	..	..	..	..	..	Placebo	5-HTP
D	..	..	..	..	..	5-HTP	Placebo
E* ..	..	..	..	..	..	5-HTP	—

* Patient E did not receive a placebo control, but a control specimen of urine was obtained.

5-HTP was dissolved in isotonic saline and administered by slow, intravenous drip over a period of approximately one hour. The rate of administration was varied to control the side-effects of nausea. The placebo isotonic saline was also given by slow intravenous drip.

INTERVIEWS

The subjects were interviewed continuously for a period of $\frac{1}{2}$ hour preceding the infusion until $1\frac{1}{2}$ hours post-infusion, and the interviews were electrically recorded. Each was also interviewed by the ward nurse on the evening of the experimental day and on the following morning by the ward psychiatrist.

Biochemical Measures: Twenty-four hour urine samples were collected on control and experimental days for each patient. Aliquots were taken for 5-hydroxy-indole-acetic acid determination by Udenfriend's method (20) and for paper chromatography. (Diet was controlled to exclude bananas which contain serotonin) (21, 22).

Methods Employed for Paper Chromatography: Aliquots of urine specimens from six patients were examined qualitatively by bi-dimensional paper chromatography. These included urines from five experimental patients and one patient who received only saline. In order to determine the urinary pattern after such injections, tests were made for both diazo-coupling and indolic substances (5-HTP, Serotonin and 5-HIAA). Twenty-two urine specimens were examined.

The urines were evaporated to a small volume on a water bath at 56° C. Seventy-five lambda amounts were spotted on Whatman #1 filter paper sheets and two-way chromatography carried out using propyl alcohol-NH₃-water (4:1:1) as the first solvent and butanol-glacial acetic-water (4:1:1) as the second solvent. The papers were air dried, examined under ultra-violet light and then stained, one set with diazotized sulfanilic acid (DSA) and another with paradimethylaminobenzaldehyde (PDAB). The spots were marked and the R_f values determined.

Psychological Measures: Immediately following the termination of the infusion each patient was tested. Tests administered included:

1. Similarities test from the Wechsler Adult Intelligence Scale (WAIS).
2. Comprehension test from the WAIS.
3. Stories from the Wechsler Memory Scale.
4. Serial association test—(the patient was given a stimulus word and asked to associate continuously to it until told to stop—after 30 seconds).

RESULTS

Chemical

All five patients excreted increased quantities of 5-HIAA, following 5-HTP administration (Table III).

TABLE III

5-hydroxy-indole-acetic Acid (5-HIAA) Excretion (in milligrams) of Patients following Placebo and 5-HTP Administration

Subject							
A	..	..	..	..	..	5-HTP	Placebo
						10.7	0.95
B	..	..	..	..	..	Placebo	5-HTP
						1.25	3.9
C	..	..	..	..	..	Placebo	5-HTP
						2.2	11.3
D	..	..	..	..	..	5-HTP	Placebo
						12.9	2.9
E	..	..	..	..	..	5-HTP	Placebo
						7.44	3.66

(6-hour urine samples—Subjects A and B.)

(24-hour urine samples—Subjects C, D, E.)

Paper Chromatography

Results. Table IV lists all the substances found in each of the urine samples examined and the frequency of their occurrence. Figure 1 shows the bi-dimensional map of these.

It will be noted that two compounds (Spot No. 8 and No. 11) were present only after 5-hydroxytryptophan injection. By comparing these R_f values against known substances, these spots were identified as 5-hydroxytryptophan and serotonin. They appeared in the 6-hour urines but not in all of the 24-hour samples. The dilution factor may be important here, since we used only 100 cc. aliquots of the 24-hour specimens. All of the test urines showed 5-hydroxy-indole-acetic acid but some of the placebo urines did also.

From the size and intensity of the spots one can estimate that a sizeable fraction of the 5-hydroxytryptophan given is excreted unchanged. It appeared in the urines two hours after injection in readily detectable amounts. The fact

TABLE IV

Compounds found in Urines of Patients

Spot No.	1 R_f 1	2 R_f 2	Ultra-Violet	DSA	PDAB	No. of Urines	Occurrence	Probable Compound
1 ..	0.15	.07	—	Yellow	—	12	Normal	—
2 ..	.42	.05	—	Red	—	13	Normal	—
3 ..	.37	.16	Yellow	—	—	16	Normal	—
4 ..	.21	.23	Clear	Colourless	—	11	Normal	—
5 ..	.52	.13	—	Red	—	15	Normal	—
6 ..	.47	.26	—	Red	—	5	Normal	Tyrosine
7 ..	.50	.21	—	Yellow	—	15	Normal	—
8 ..	.47	.26	—	Blue Red	Pink Orange	8	After 5-HT only	5-Hydroxytryptophan
9 ..	.64	.38	Dark	Blue Red	—	7	Normal	—
10 ..	.28	.38	—	Orange	—	4	Normal	—
11 ..	.70	.35	Green	Brown Red	Blue Purple	6	After 5-HT only	5-Hydroxytryptamine (Serotonin)
12 ..	.69	.48	—	Red	Pink Orange	3	Normal	Indican
13 ..	.58	.40	Yellow	—	Yellow	16	Normal	Urea
14 ..	.39	.44	Blue	—	—	11	Normal	—
15 ..	.71	.52	—	Orange	Orange	17	Normal	—
16 ..	.86	.61	—	Red	—	10	Normal	—
17 ..	.12	.63	Blue	—	—	8	Normal	—
18 ..	.42	.61	—	Pink Orange	—	10	Normal	5-Hydroxy-indole-acetic acid
19 ..	.53	.78	—	Orange	Pink	15	Normal	—
20 ..	.62	.83	—	Orange	—	13	Normal	—
21 ..	.66	.89	—	Blue Red	Purple	14	Normal	—
22 ..	.37	.75	—	Pink	—	4	Normal	—
23 ..	.56	.88	—	—	Pink	3	—	—
24 ..	.79	.88	Yellow	Yellow	Yellow	15	Normal	—

1. Propyl Alcohol-Ammonia-Water (4:1:1) Solvent 1.

2. Butanol-Acetic Acid-Water (4:1:1) Solvent 2.

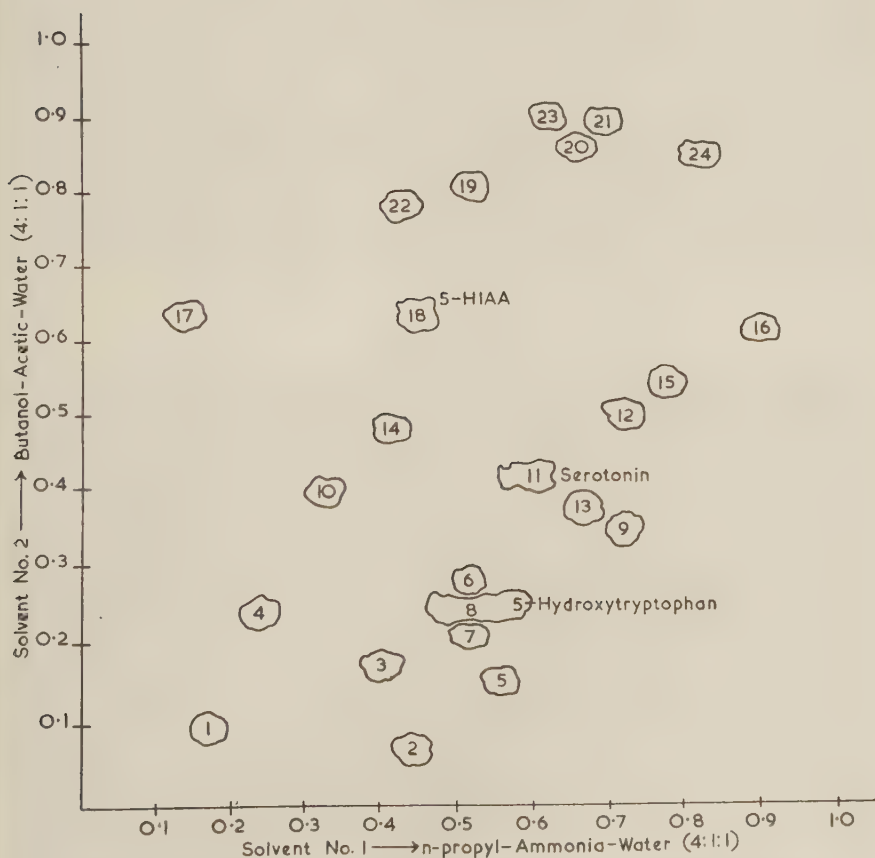


FIG. 1.—Bi-dimensional Chromatographic Map of Diazo-coupling Compounds.

that serotonin also appeared in these same urines would augment the hypothesis that the 5-H tryptophan had been converted to serotonin.

Psychological Effects

In only one of the 5 subjects (Subject A) were there definite psychological effects following the 5-HTP infusion. This subject was one whose acute psychosis had included olfactory hallucinations. After she had received about half the infusion the patient complained of increased nervousness, a fluttering in her stomach and a ringing in her ears. She then complained of a "musty" odour in the room as though it needed airing. She remarked that all of these symptoms were reminiscent of those she had experienced at the onset of her psychosis, some months earlier. As the infusion was continued these symptoms all increased in severity. In particular she felt more tense and the smells seemed stronger. In addition to the musty odour she also reported smelling ether. For a brief period the patient showed a tendency to confuse one of the experimenters with her husband and was uncertain whether or not the odours were "real". Along with these symptoms she showed an increase in psychomotor activity, and some pressure of speech with a tendency toward disorganization and scattering of thought. Psychological tests also revealed scattering of thought and looseness of association, in addition to impairment of concentration and immediate memory. These effects reached a peak at about the time the infusion was terminated because of vomiting within an hour. After the infusion was discontinued these effects all disappeared within an hour. Subjectively and objectively the patient had returned to her pre-drug state. She explained all her symptoms on the basis of the drug—and had no further recurrence of symptoms.

On the following week, when she received saline placebo the patient manifested increased anxiety but none of the other symptoms.

None of the other four subjects showed definite psychological effects from either drug or placebo, although Subject B indicated a slightly greater reluctance to talk after 5-HTP and showed mild impairment in concentration and memory on testing. These effects were not striking.

DISCUSSION

The increased 5-HIAA excretion found in the urines following the 5-HTP infusions as well as the results of paper chromatography provide evidence that much of the 5-HTP administered was converted to serotonin. As we have mentioned earlier, brain serotonin levels are increased by 5-HTP administration.

When viewed alone, patient (A) seems to offer dramatic evidence of the "schizophrenogenic" effects of 5-HTP, or more correctly, of increased levels of brain serotonin, in predisposed individuals. The result is particularly interesting in view of the olfactory hallucinations which were involved. The patient is one with a history of olfactory hallucinations, which recurred during the 5-HTP administration. It has been shown that serotonin is found in relatively high concentrations in the rhinencephalon (23), and according to Costa (24), concentrations are particularly high in the anterior perforated substance, uncus, hippocampal gyrus and in the subcallosal gyrus. This portion of the brain, the old "nose brain" is involved not only in olfactory perception, but apparently in a variety of other processes, including emotion (25, 26, 27, 28). One would be tempted to speculate whether this patient's mental illness involved a disorder of serotonin metabolism in the rhinencephalon or limbic system. Such an hypothesis fits nicely with the experimental effect of 5-HTP in this patient.

Before speculating further, however, the other four, negative, results which are quite sobering, must be considered. We must ask whether the symptoms produced in patient (A) could have resulted from factors other than the 5-HTP. It is indeed quite possible that they did. Despite the fact that "double-blind" procedure was followed, the patient and the experimenters had no difficulty in telling when she had 5-HTP, because of its side-effects. It is, of course, well known that a wide variety of psychological changes, including psychotic symptoms may occur in some persons as a result of psychological influences such as fear, or suggestion. The conscious or unconscious expectations of patient or doctor in particular may operate suggestively. One patient who was asked to be a subject for this study refused, and had a brief recurrence of her paranoid psychosis, apparently in response to the threat of being experimented upon.

The question of whether patient (A's) symptoms were actually due to 5-HTP or to other factors might have been settled by continued study of the patient, but unfortunately due to circumstances beyond the authors' control she was discharged from the hospital several days after the initial studies.

We are left with two alternative explanations of the results. If we consider the possibility that 5-HTP was really effective in patient (A) and not in the other four, we must also assume that there is a fundamental chemical difference between this patient and the others. This presumably could consist of a disorder in serotonin metabolism in patient (A), that was either lacking, or not present to the same degree in the other four. As an alternative many would logically point to the four negative results and discount the reaction of subject (A) as an artifact.

The authors do not feel that the evidence justifies a choice of either explanation. This complicated, but intriguing question, can be settled only by further study. In addition to further studies with mental patients, studies in animals with recording electrodes implanted in the limbic system during 5-HTP administration might be enlightening.

SUMMARY

In order to observe the effects of increased brain serotonin levels, four hospitalized schizophrenics and one depressed patient with some schizophrenic features were given 5-hydroxytryptophan intravenously in doses of 80 mg. to 100 mg. The patients chosen were females, in remission from their illness, who volunteered as subjects. Each patient also received a control infusion of placebo. Urine samples were collected for 5-HIAA determinations and paper chromatography on all patients. All patients showed increased excretion of 5-HIAA and serotonin following 5-HTP infusion. One of the five patients showed significant psychiatric effects following her 5-HTP infusion. This patient, a paranoid schizophrenic, in remission, with a history of olfactory hallucinations had a recurrence of many symptoms, including olfactory hallucinations, during the infusion. Psychological tests showed disorganization and scattering of thought accompanying these symptoms. The effects wore off within an hour after the 5-HTP infusion was discontinued.

The other four patients manifested no significant psychological effects from the 5-HTP.

The question of whether or not this reaction can be attributed to the 5-HTP is considered.

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THE EFFECT OF CHLORPROMAZINE ON THE INCIDENCE OF EPILEPTIC PHENOMENA DURING INSULIN COMA THERAPY

A STATISTICAL INVESTIGATION

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EPILEPTIC manifestations complicating insulin coma therapy (I.C.T.) were described by Sakel in his original paper (1937). In recent years the administration of chlorpromazine to patients undergoing I.C.T. has been common practice. Lancaster and Jones (1954), however, have commented on the resulting apparent increase in the incidence of epileptic fits.

The effect of chlorpromazine on the convulsive threshold has been the subject of a number of investigations, The conclusions derived from these are sometimes conflicting and will be reviewed below. While some experimental studies on this subject have been controlled, all the clinical reports have been based solely on clinical impressions.

AIM OF INVESTIGATION

In the following investigation, we set out to enquire whether chlorpromazine increased the incidence of epileptic manifestations during I.C.T. and furthermore whether the addition of anti-convulsant drugs reduced such incidence.

MATERIAL AND METHOD

Seventy consecutive non-epileptic schizophrenic patients admitted to the Insulin Unit of the Bethlem Royal and Maudsley Hospitals, between January, 1957 and December, 1958 were included in this study. The author had been responsible for the supervision of treatment in the above unit during this time and his duties included the supervision of the daily records of treatment kept by the nursing staff. Each day the various features of the coma were charted fully and amongst other information kept was the incidence of epileptic manifestations and the time of their occurrence. These notes were examined each day prior to prescribing the dose of insulin for the following day.

During the course of these 2 years, combined insulin and chlorpromazine therapy was introduced, and for a time all patients received this treatment. Chlorpromazine rendered the patients more manageable and improved the therapeutic atmosphere of the ward. Clinical observations, however, suggested that the combined treatment increased the frequency of epileptic manifestations. After an 18-year old schizophrenic patient had fractured a thoracic vertebra in a particularly violent fit, it was decided that anti-convulsants, in the form of sodium hydantoin $1\frac{1}{2}$ gr. three times daily, should be administered routinely to all our patients.

Our 70 patients therefore fell into three distinct groups:

1. 40 patients who received insulin alone.
2. 10 patients who received insulin and chlorpromazine.
3. 20 patients who received insulin, chlorpromazine and phenytoin (sodium hydantoin).

RESULTS

TABLE I

Incidence of Epileptic Manifestations

	Insulin Alone	Insulin and Chlorpromazine	Insulin, Chlorpromazine and Phenytoin
Number of patients	40	10	20
Total number of comas ..	1,519	377	759
Total number of fits	72	37	16

When our findings, shown in the above table, are submitted to statistical analysis using the χ^2 technique, the difference in the incidence of epileptic manifestations in the three groups was found to be significant at a level greater than 1 per cent.

Examination of the distribution of epileptic manifestations in our three groups of patients gives further support to the above findings.

TABLE II

Distribution of Epileptic Manifestations

	Number of Fits				Insulin Alone	Insulin and Chlorpromazine	Insulin, Chlorpromazine and Phenytoin
0	..	..	..	..	20	0	12
1-3	..	..	..	..	13	6	6
4-6	..	..	..	..	3	3	2
7	..	..	..	..	4	1	0
Total	..	..	..	..	40	10	20

There was no relationship between the dose of chlorpromazine or insulin administered and the incidence of fits. There was no tendency for epileptic manifestations to occur at any particular stage of the treatment in the different groups.

DISCUSSION

The possibility that spontaneous epileptic attacks during I.C.T. were desirable and of good prognostic significance was entertained by Sakel (1937). Not all investigators, however, found themselves in agreement with him. Plattner and Frolicher (1938) stated that epileptic manifestations occurred in 1.6 per cent. of cases that recovered and in 4.3 per cent. of cases that did not. A higher incidence of epileptic manifestations was reported by Gross-May (1938): in his experience, 35 per cent. of patients undergoing I.C.T. had epileptic fits at some stage of the treatment. Tennent (1944) warned of the danger of fractures occurring as a consequence of epileptic fits in I.C.T. Leibermann and Hoenig (1953), however, concluded from their study that epileptic activity

witnessed either as seizures or as myoclonic jerks during insulin coma treatment was of good prognostic significance.

Epileptic manifestations in I.C.T. may occur in the early or late stages of hypoglycaemia or during the later stages of coma and are attributed to the individual sensitivity of the cortex to hypoglycaemia. Hill (1948) reported the case of a patient with a marked tendency to produce EEG abnormalities when activated by insulin. He studied this patient in detail over a period of 12 weeks and found that the amount of paroxysmal activity was greatest at the beginning and at the end of stupor at which times two spontaneous convulsions occurred.

Leibermann and Hoenig (1953) studied the photometrazol threshold in a group of catatonic schizophrenics and found that this was lower than in the normal population, the lowest levels being found during emergence from stupor. They put forward a hypothesis as a result of their study, to the effect that there is a dynamic relationship between the tendency to discharge on the part of the diencephalic mechanisms as measured by the convulsive threshold, and the clinical state. Leibermann and Hoenig's hypothesis is in agreement with Gellhorn (1943). The latter, from observations of an A.N.S. regulating centre following successful physical treatment of schizophrenia, deduced that in this disease there is a variation in the reactivity of a central mechanism which functions through the sympathetic-adrenal and vaso-insulin systems. Both Gellhorn and Hill (1957) suggest that this central mechanism is a diencephalic autonomic centre.

Chlorpromazine, the earliest phenothiazine derivative to be used widely in neuropsychiatry, is said to exert its action through a depression of the spontaneous activity of the brain-stem reticular formation, which may be related to its anti-adrenaline properties (Hiebel *et al.*, 1954; Longo *et al.*, 1954; Bradley and Hance, 1957).

Courvoisier *et al.* (1953) stated that in animal experiments chlorpromazine showed anti-convulsant properties but, though some later investigators confirmed their findings, others reported that chlorpromazine lowered the epileptic threshold in animals (Heming *et al.*, 1956). Tedeschi and his co-workers (1958) report that chlorpromazine affects the "minimum E.C.T." threshold of mice over a narrow range of dosage only, i.e. oral doses of between 9 mg./Kg. and 27 mg./Kg. They state moreover that these properties are particular to chlorpromazine and are not shared by other phenothiazine derivatives. Studies by Lehmann and Hanrahan (1954) had demonstrated a lowered convulsive threshold following administration of chlorpromazine to psychiatric patients.

More recently Bradley and Jeavons (1957) studied the effect of chlorpromazine and reserpine on the "convulsant" and "sedation" threshold of 12 chronic schizophrenics. Neither drug proved to have any demonstrable effect on the convulsive threshold as measured by the hexazol method (Ulett *et al.*, 1955). They discuss their findings and put forward possible explanations to account for them. According to the authors it is possible that the mechanism through which experimental and spontaneous convulsions are produced, may not be the same. This hypothesis would explain the discrepancy between their findings and previous clinical observations. It does not explain, however, the essential difference between their results and those of previous investigators who have studied the same problem.

From the clinical angle the findings of Lomas *et al.* (1955), Kinross-Wright (1955), Schlichter *et al.* (1956), Tarjan (1957) and others, revealed an increased incidence of epileptic seizures in established epileptics and the occurrence of fits for the first time in hitherto non-epileptic patients, following administration of

chlorpromazine. The above authors recommended that the drug should not be regarded as a substitute for anti-convulsants, a warning of particular importance since Bonafede (1955) and others had reported favourably on the use of chlorpromazine in the treatment of behaviour disorders in epileptics.

The epileptogenic properties of this drug which may lead to the development of manifest fits in susceptible people, can be counterbalanced by the potentiating effect on anti-convulsant drugs as well as by a reduction in emotional tension (Meszaros and O'Reilly, 1956; Rudy *et al.*, 1956; Feldman, 1957; Voegelé and May, 1957). In a paper on the use of chlorpromazine in the management of patients with head injury, Shea *et al.* (1955) found that convulsions could be controlled by halving the previous dose of cortical depressants once chlorpromazine was added to them.

Electro-encephalographic studies after administration of chlorpromazine are inconclusive. Terzain (1952) reported an increase in amplitude or normal rhythm and the re-appearance of well-organized alpha rhythm, Azima (1954) could find no specific changes and Lehmann and Hanrahan together with Shagass (1955) only found changes secondary to drowsiness. Fabisch (1957) states that in patients with an unstable inter-seizural record there is an increase in abnormal EEG phenomena after administration of intravenous chlorpromazine. This effect is similar to that produced by hyperventilation or photic stimulation. Szatmari (1956) reports increased sensitivity to hyperventilation as well as decreased metrazol threshold after chlorpromazine in epileptic patients.

The relationship between chlorpromazine and epilepsy can be seen to be an extremely complicated one, complicated further by the assumption put forward by Gibbs (1951) that there is an antithesis between seizures and non-ictal psychiatric disorders.

The value of our own study is limited in that our patients were schizophrenic and undergoing insulin therapy; two additional variables were thus introduced. Our results, however, demonstrate convincingly that in such patients chlorpromazine has epileptogenic properties and that the combination of chlorpromazine and sodium hydantoin greatly reduces the incidence of fits in treatment. We are unable to deduce from our data whether the combination of chlorpromazine and sodium hydantoin is more effective than the latter drug alone in diminishing the incidence of fits.

SUMMARY

The incidence of epileptic manifestations occurring as a complication of Insulin Coma Therapy is compared in three groups of patients receiving (a) insulin alone, (b) insulin and chlorpromazine, and (c) insulin, chlorpromazine and sodium hydantoin. Our results, statistically significant at the 1 per cent. level, show that in such patients chlorpromazine has epileptogenic properties.

The literature on the relationship between epilepsy and chlorpromazine is discussed.

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THE EFFECTS OF MEPROBAMATE ON PERCEPTION

I. APPARENT MOVEMENT

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INTRODUCTION

A NUMBER of recent studies of apparent movement have been designed with Kohler and Wallach's satiation theory or some similar theory of cortical processes as their basis. The work has been reviewed in some detail (4) and we shall concern ourselves here only with those studies that are both less equivocal and directly relevant to the present study.

Weiskrantz (5) produced evidence suggesting that a stationary inspection figure can affect apparent movement to the extent of altering the length of its pathway. Inspection figures (two black rectangles) placed between the stimuli for apparent movement (two dots) resulted in an apparent lengthening of the path of the moving dot. Since by Korte's law t_{opt} varies with s (i.e. the time interval between the lights varies with the distance between them) one would predict that t would increase under Weiskrantz's conditions. Though Weiskrantz does not say anything about this, Deatherage (2) reports a study on the effects of prolonged inspection of apparent movement. If one can consider apparent movement as resulting from a process in the cortex corresponding to the line of movement, then, since satiation results in a functional increase in distance between the stimuli, prolonged inspection of apparent movement should lead to a functional increase in the distance between the stimuli. This by Korte's law should result in an increase in t_{opt} . This is what Deatherage found.

Brenner's finding (1) that four kinds of continuous stimulation (*i*) visual, (*ii*) auditory, (*iii*) voluntary movement and (*iv*) simple mental arithmetic, resulted in an increase in t when studying the upper threshold (the threshold between simultaneity and movement) makes an explanation in terms of direct isomorphic relations between perception and cortical events, difficult. But the findings, certainly with regard to the effects of visual continuous stimulation, do fit in with the other studies reported above.

There is some evidence from work in this department that meprobamate acts as a central nervous system depressant. It was decided to study the effects of meprobamate on apparent movement in order to test the drug action hypothesis advanced by Eysenck in a previous paper (3). The hypothesis stated that stimulant drugs increased excitatory potential and decreased inhibitory potential, while depressant drugs decreased excitatory potential and increased inhibitory potential. If depressant drugs increase inhibitory potential, then one would predict that the upper threshold for apparent movement would be lowered, i.e. the threshold between simultaneity and movement would occur at longer time intervals.

METHOD

The Withers direct exposure tachistoscope (6) and an electronic cycling timer were used. The time interval between the stimuli could be varied from 30–2,500 ms. The exposure time was 45 ms. The stimulus figure used was a simple one, two circles of light $\frac{1}{2}$ cm. in diameter and $3\frac{1}{4}$ cm. apart. The distance of the stimulus figure from the rubber eyepiece was 21 inches. Further details about the tachistoscope and timer can be found in Wither's paper.

Preliminary work with the apparatus revealed the same difficulties encountered by Brenner (1) in obtaining a satisfactory lower threshold, i.e. between succession and movement, and this study deals only with the upper threshold, i.e. between simultaneity and movement.

After a number of practice trials to familiarize the subject with the apparent movement phenomenon, the subject was given the following instructions: "In a few moments I shall ask you to look into the viewing tube. You will see two lights flickering on and off simultaneously, or one light appearing to move to and fro in front of you. I want you to say 'Now' whenever you see a change from simultaneity to movement or from movement to simultaneity".

The time interval at which the subject said "Now" was recorded in milliseconds as the upper threshold. Four trials were given and the limiting method was used. Ascending and descending trials were alternated with each other. The means of the four trials constituted the threshold for that session.

Each subject was given two treatments, (i) placebo, (ii) 600 mg. meprobamate on two different days, the order of treatments being counterbalanced. Both the placebo and meprobamate were in identically appearing tablet form and taken orally.

On each day the subject was given one session before treatment (initial session) and four sessions 1, $2\frac{1}{2}$, $3\frac{1}{2}$ and $4\frac{1}{2}$ hours after administration of the drug or placebo.

SUBJECTS

The total N in this experiment was six. All were female subjects. The ages of the sample ranged between 25 and 45 with a mean of 35.3.

RESULTS

Table I shows the results of an analysis of variance carried out to test the significance of the differences between the scores. It will be seen that two significant F ratios emerge, namely, those "Subjects" and "Treatments".

TABLE I

Source	Degree of Freedom	S. Squares	Mean Squares	F	P
Subjects	5	7465.188	1493.038	11.573	.001
Times	3	564.563	188.188	1.459	N.S.
Treatments	1	1230.188	1230.188	9.536	.01
Subject/Time	15	1625.062	108.337	—	N.S.
Treatment/Time	3	299.062	99.687	—	N.S.
Subject/Treatment	5	1589.187	317.837	2.464	N.S.
Residual	15	1935.063	129.004		
Total	47	14708.313			

Figure 1 shows the results in diagrammatic form. It is noteworthy that though the subjects were tested at intervals up to $4\frac{1}{2}$ hours after administration of the treatment, the treatment/time interaction is not significant.

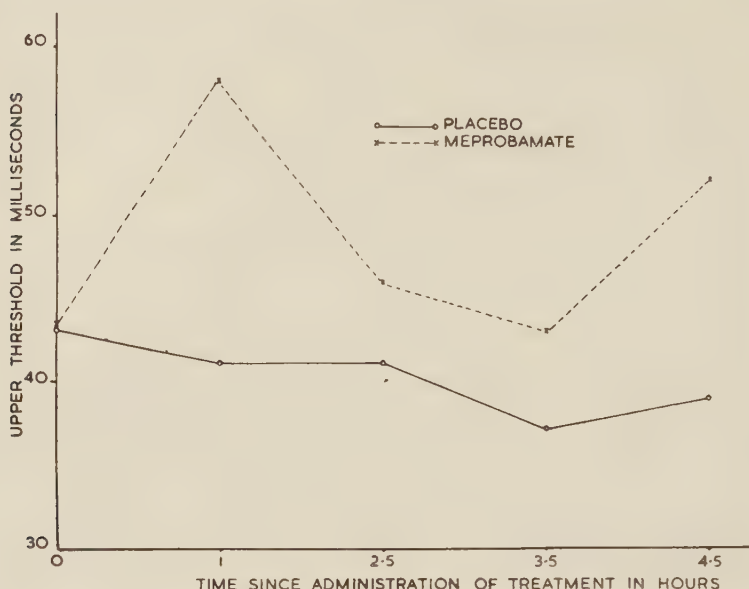


FIG. 1.—The upper threshold of apparent movement (simultaneity-movement) in milliseconds for a group of subjects under drug treatment.

The significant differences indicate that considerable differences exist between people in the upper threshold for apparent movement and that, as predicted, meprobamate lowers the threshold, i.e. the change from apparent simultaneity to apparent movement occurs at longer time intervals.

An extensive investigation on the effects of two dosages of meprobamate (600 mg. and 1,200 mg.) on apparent movement is under way.

SUMMARY

Six subjects were tested under two conditions each on two separate occasions. The two conditions were: (i) administration of placebo, (ii) administration of 600 mg. meprobamate. Testing on each day was done once before administration of the treatment and 1, $2\frac{1}{2}$, $3\frac{1}{2}$ and $4\frac{1}{2}$ hours after administration.

The results showed that, as predicted, meprobamate lowers the upper threshold of apparent movement.

ACKNOWLEDGMENTS

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THE EFFECTS OF MEPROBAMATE ON PERCEPTION

II. THE VISUAL AFTER-IMAGE

By

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THERE is no discussion in Stevens' (16) or Osgood's (14) textbooks of experimental psychology of the contribution of cortical functions to the production of visual after-images. Woodworth (19) presents a theory of after-images involving the cortex in the first edition of his book. It is not repeated in the second edition. There is, however, a large number of reported studies indicating the importance of cortical functions in the production of after-images (e.g. 1, 3, 6, 9, 11, 12, 13, 15, 17). In view of these studies it was decided to use the after-image in a further attempt to verify or disprove the drug action hypothesis advanced by Eysenck in a previous paper (2). This hypothesis stated that stimulant drugs increased excitatory potential and decreased inhibitory potential, while depressant drugs decreased excitatory potential and increased inhibitory potential.

Though after-images have been discussed in terms of some kind of excitatory and inhibitory potential (5, 10) there is no generally accepted explanation of the phenomena. There are, however, two reported observations which appear to fit into the general theory of cortical-excitation-inhibition.

Levine and Graham (9) used for the stimulus patch a small opening forming a visual angle of 17' with the eyes of the subject who sat 1.5 m. away. The opening was covered with milk glass and the intensity of illumination was kept constant at about 0.4 ml. The stimulation time was 15 seconds. A larger opening subtending a visual angle of 44' and separated from the small opening by a visual angle of 1° 42' served as an inducing patch. The intensity of its illumination was varied in a random order and the illumination remained on throughout the 15 seconds stimulation by the stimulus patch and until the subject reported the appearance of the after-image of the stimulus patch. It was found that as the intensity of the inducing patch increased, the latency of the after-image for the stimulus patch decreased. It was argued that the shortening of the latency could not be explained in terms of summation of excitations from an adjacent excited region with the effects from the stimulated region since it had been found that increasing the intensity of the stimulus-patch itself resulted in an *increase* in the latency of the after-image (7). Levine and Graham explained their results in terms of inhibition by the inducing patch of the *positive* processes preceding the *negative* after-effect produced by the stimulus patch.

Since depressant drugs are postulated to decrease excitatory potential, one would predict that meprobamate, which has been shown in this department to act as a central nervous system depressant, would shorten the latency of the after-image.

Klein and Krech (8) refer in one of their papers to an unpublished report by Klein to the effect that where persistence of the after-image was measured as a function of the duration of stimulus exposure, it appeared that for longer exposures the duration of the after-images in brain-injured fell off significantly as compared with non-brain-injured. They discuss this finding in terms of *satiation* attributes which they postulate to be characteristic of individuals with a lowered basal cortical conductivity, e.g. brain-injured.

Eysenck (4) has prepared a detailed theoretical formulation in an attempt to mediate the relationships between the length of visual after-effects (including the after-image) on the one hand and personality features, drug effects and brain damage on the other. On the basis of his theory he predicts that depressant drugs would shorten the duration of the after-image.

On the basis of the drug postulate, the findings of Levine and of Klein and Eysenck's theoretical formulation, it was predicted that the latency and the duration of the after-image would be decreased by the administration of meprobamate.

METHOD

The stimulus was a red square 5 cm.² with a black focusing point in the centre. The red square surrounded by black opaque paper was attached to a sheet of perspex which was inserted into the end of the viewing tube of a Wither's tachistoscope (18). Two 5W neon lamps behind the perspex illuminated the red square during the stimulation period. All testing was done in a darkened room.

After a number of preliminary trials to familiarize the subject with the after-image phenomenon, she was given a three-minute rest period. She was then given the following instructions: "In a few moments I shall ask you to look into the viewing tube. The red square will appear and I want you to focus your eyes on the black spot in the centre. After thirty seconds the red square will disappear. As soon as the after-image appears, I want you to press the telegraph key on your right. As soon as the after-image disappears release the key. The after-image may appear and disappear a number of times. Remember—as long as the after-image is there, keep the key pressed down—as long as there is no after-image the key must be released."

The subject was then told to look into the viewing tube and the red square was illuminated. At the end of thirty seconds the illumination was switched off and a mark was made simultaneously on the recording chart of an Evershed and Vignoles recorder travelling at a speed of one inch every five seconds. Activation of a second event marker by the telegraph key controlled by the subject recorded the appearances and disappearances of the after-image. When the after-image had completely disappeared the subject was told to rest for three minutes and was then given a second trial.

Two scores were used in the present investigation (*i*) the latency period, i.e. the time from the end of stimulation by the red square to the appearance of the first after-image. (*ii*) The total duration of the after-effect, i.e. the time from the end of stimulation by the red square to the disappearance of the last after-image. The means of the two trials constituted the score for that session. The recording method permitted accuracy to the nearest quarter of a second.

Each subject was given two treatments (*i*) placebo, (*ii*) 600 mg. meprobamate on two different days, the order of treatments being counterbalanced. Both the placebo and meprobamate were in identically appearing tablet form and taken orally.

On each day the subject was given one session before treatment (initial session) and four sessions 1, $2\frac{1}{2}$, $3\frac{1}{2}$ and $4\frac{1}{2}$ hours after administration of the drug or placebo.

SUBJECTS

The total N in this experiment was six. All were female subjects. The ages of the sample ranged between 25 and 45 with a mean of 35.3.

RESULTS

Tables I and II show the results of analyses of variance carried out to test the significance of the differences between the latency and total duration scores for the two treatments. It will be seen that five significant F ratios emerge, namely, those for "Subjects" and "treatments" in the case of both latency and duration and the interaction between "subjects" and "treatment" in the case of total duration. Figures 1 and 2 show the results in diagrammatic form.

The significant differences indicate (i) that considerable differences exist between people in the latency and total duration of the after-image, (ii) that meprobamate as predicted decreases the latency and total duration, and (iii) that there are differences between people in the effect of meprobamate on the total duration of the after-image. It is noteworthy that though the subjects were tested at intervals up to $4\frac{1}{2}$ hours after administration of the treatment the treatment/time interactions are not significant. An extensive investigation on the effects of different dosages of meprobamate over a longer period of time is under way.

TABLE I

Analysis of Variance of Latency Scores

Source	Degree of Freedom	S. Squares	Mean Squares	F	P
Subjects	5	362.798	72.56	7.088	.005
Time	3	6.352	2.117	—	N.S.
Treatments	1	60.021	60.021	5.863	.05
Subject/Time	15	79.788	5.319	—	N.S.
Treatment/Time	3	15.571	5.190	—	N.S.
Subject/Treatment	5	65.110	13.022	1.272	N.S.
Residual	15	153.560	10.237	—	N.S.
Total	47	743.200			

TABLE II

Analysis of Variance of Total Duration Scores

Source	Degree of Freedom	S. Squares	Mean Squares	F	P
Subjects	5	7445.66	1489.132	41.463	.001
Time	3	147.839	49.280	1.372	N.S.
Treatments	1	784.083	784.083	21.832	.001
Subject/Time	15	465.114	31.008	—	N.S.
Treatment/Time	3	219.384	73.128	2.036	N.S.
Subject/Treatment	5	788.807	157.761	4.393	.05
Residual	15	538.726	35.915		
Total	47	10389.613			

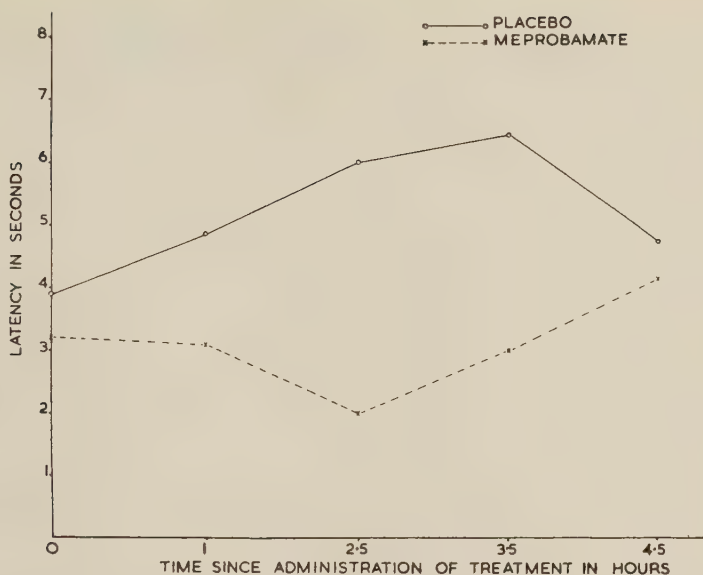


FIG. 1.—Latency of the visual after-image in seconds for a group of subjects under drug treatment.

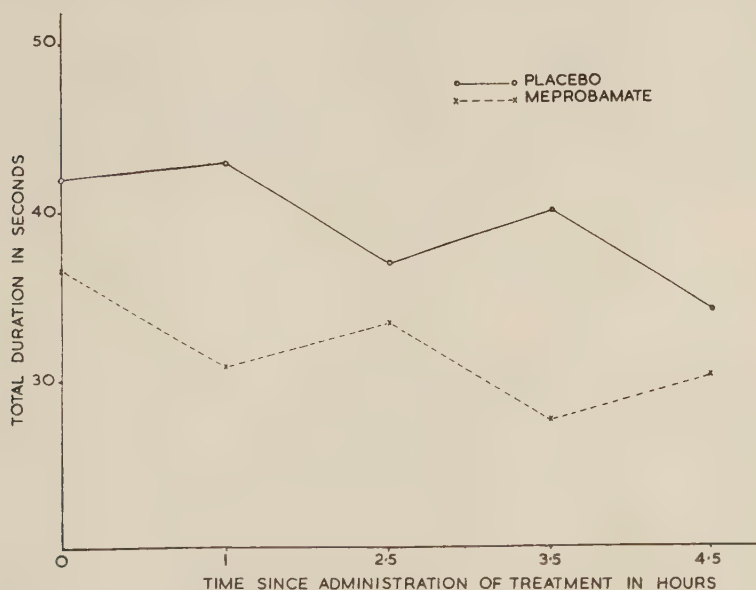


FIG. 2.—Total duration of the visual after-image in seconds for a group of subjects under drug treatment.

SUMMARY

Six subjects were tested under two conditions each on two separate occasions. The two conditions were: (i) administration of placebo, (ii) administration of 600 mg. meprobamate. Testing on each day was done once before administration of the treatment and 1, $2\frac{1}{2}$, $3\frac{1}{2}$ and $4\frac{1}{2}$ hours after administration.

The results showed that both the latency and the total duration of the after-image were decreased after administration of the meprobamate.

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THE EFFECTS OF MEPROBAMATE ON PERCEPTION

III. THE SPIRAL AFTER-EFFECT

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A REVIEW of the history and experimental findings relating to the spiral after-effect can be found elsewhere (5) and will not be repeated here. The reliability of the after-effect, the major role played by the cortex in its production and the evidence already obtained that the after-effect is modifiable in accordance with Eysenck's drug action hypothesis (2) indicated it to be a promising test in the investigation into the effects of meprobamate on perception.

The drug action hypothesis states that stimulant drugs increase excitatory potential and decrease inhibitory potential, while depressant drugs decrease excitatory potential and increase inhibitory potential (3).

Eysenck (4) has prepared a detailed theoretical formulation in an attempt to mediate the relationships between the length of visual after-effects (including the spiral after-effect) on the one hand and personality features, drug effects and brain damage on the other. On the basis of his theory he predicts that depressant drugs would shorten the duration of the spiral after-effect.

Meprobamate having been shown to act as a central nervous system depressant (4), it is predicted that the spiral after-effect would be decreased by the administration of meprobamate. Two studies were conducted to test this prediction.

STUDY I

METHOD

The spiral used in both studies is a four-throw spiral of 180° . It is $8\frac{1}{4}$ inches in diameter and is rotated by a variable speed electric motor controlled through a rheostat. The speed of rotation is set by means of a multiple speed strobe disc built into the back of the housing. The speed used in both studies was 100 r.p.m.

Illumination for the spiral was provided by a 60-watt and 40-watt bulb mounted on a laboratory stand 12 inches from the front of the spiral.

It was found in preliminary experiments reported elsewhere (1) that a photograph of the spiral placed close to the subject tended to produce more reliable results, when used as a projection field, for the after-effect, than when the spiral itself was used as the projection field.

The projection field in both these studies was a photograph of the spiral mounted on stiff black cardboard which was attached to the wall at the right of the subject. The photograph was 3 inches in diameter and the distance from the subject was 27 inches. Thus, the photograph subtended a visual angle equal to that subtended by the spiral which was 6 feet from the subject. An adjustable chin rest ensured that the same distance was maintained from both the spiral and the photograph throughout the studies. Illumination for the photograph was provided by a 40-watt lamp 1 foot away.

After a preliminary trial to familiarize the subject with the after-effect, the following instructions were given: "In a few seconds I shall ask you to close your eyes and I shall set the spiral rotating. When I say 'Ready!' I want you to rest your chin on the chin rest, facing the spiral but with your eyes still closed. When I say 'Now!' open your eyes and fixate the screw in the centre of the spiral. After one minute, the spiral will stop rotating, the lights in front of the spiral will go out and the light on your right will come on. At that point, I want you to turn, keeping your chin on the chin rest, and look at the photograph of the spiral. You will experience an after-sensation of movement. It may be an expansion effect or contraction effect coupled with rotation in the opposite direction. When all the movement has stopped, say 'Now!'."

The length of the after-effect was timed by a stop watch.

Two trials were given—a "contraction trial" followed by an "expansion trial"*. There was a one-minute rest pause between the two trials.

Each subject was given two treatments (1) placebo, (2) 400 mg. meprobamate on two different days, the order of treatments being counter-balanced. Both the placebo and meprobamate were in identically appearing tablet form and taken orally.

On each day the subject was given one session before treatment (initial session) and nine sessions $\frac{1}{2}$, 1, $1\frac{1}{2}$, 2, $2\frac{1}{2}$, 3, $3\frac{1}{2}$, 4, $4\frac{1}{4}$ hours after treatment.

In order to investigate the relationship between fixation and length of the after-effect, a test of fixation devised by Holland who presents the rationale for it elsewhere (5) was given immediately after the initial readings of the after-effect and $\frac{1}{4}$, $1\frac{3}{4}$, and $3\frac{3}{4}$ hours after administration of the treatment.

The test consists of rotating the spiral at 600 r.p.m. Any eye movements whether voluntary or involuntary, or due to blinking, produces on the uniform greyness of the disc a "flash" in which part of the spiral emerges and can be seen clearly for a fraction of a second.

The subject was told to fixate the screw in the centre of the spiral which was rotated at 600 r.p.m. for one minute. The number of "flashes" was recorded by means of a telegraph key which the subject pressed for each flash. The key was connected with an Evershed and Vignoles recorder travelling at a speed of one inch every five seconds.

SUBJECTS

The total N in this study was six (four male, two female). They were all post-graduate students of psychology. The age range was from 25 years to 37 years, with a mean of 30.0 years.

RESULTS

Table I shows the results of an analysis of variance carried out to test the significance of the differences between the spiral after-effect scores. It will be seen that two significant F ratios emerge, namely, those for "Subjects" and "Treatments". Figure 1 shows the results in diagrammatic form. It is noteworthy that though the subjects were tested at intervals up to $4\frac{1}{4}$ hours after administration of the treatment, the treatment/time interaction is not significant.

The significant differences indicate that considerable differences exist between people in the spiral after-effect and that, as predicted, meprobamate shortens the length of the after-effect.

* An "expansion trial" is one where a forward rotation of the spiral is followed by an after-effect of expansion. A "contraction trial" is one where a reverse rotation of the spiral is followed by an after-effect of contraction.

TABLE I

Source	Degree of Freedom	S. Squares	Mean Squares	F	P
Subjects	5	3689.684	737.94	411.34	< .001
Treatments	1	9.976	9.976	5.56	< .025
Times	9	11.880	1.320	—	N.S.
Subject/Time	45	60.862	1.352	—	N.S.
Treatment/Time	9	13.879	1.542	—	N.S.
Subject/Treatment	5	8.388	1.678	—	N.S.
Residual	45	80.730	1.794	—	
Total	119	3875.399			

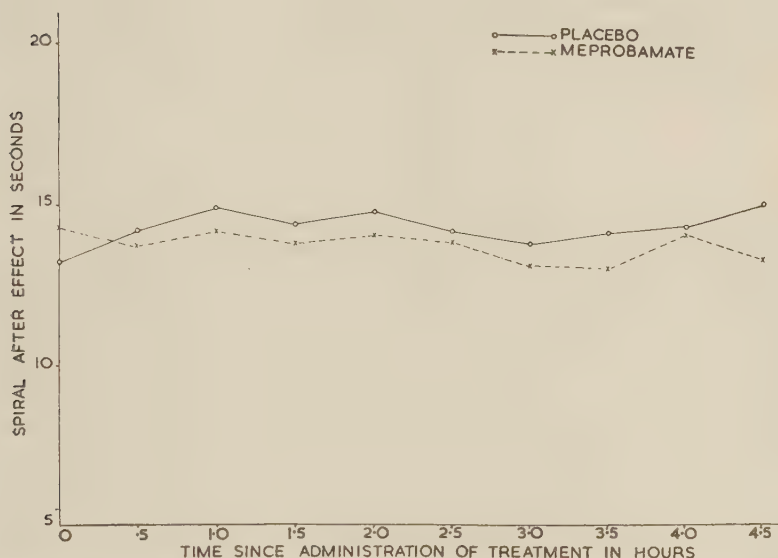


FIG. 1.—Duration of the spiral after-effect in seconds for a group of subjects under drug treatment (Study I).

It may be argued that the drop in the after-effect after administration of meprobamate is due to poorer fixation since this drug is a muscle relaxant. Insofar as Holland's fixation test described above is a valid measure, one would expect both a significant negative correlation between the length of the after-effect and the number of flashes on the fixation test and an increase in the number of flashes after administration of the drug.

The product moment correlation coefficient was calculated for six initial after-effect scores (mean of two trials) and six fixation scores obtained at the same initial session— $r = -.35$ which is not statistically significant. Table II

TABLE II

	Drug Day	Placebo Day
Initial session	20.166	16.333
$\frac{1}{4}$ hour after administration of treatment ..	20.333	19.166
$1\frac{3}{4}$ hours after administration of treatment	17.500	17.500
$3\frac{3}{4}$ hours after administration of treatment	17.166	19.000

showing the mean fixation scores for the six subjects at the four sessions on both drug day and placebo day clearly indicates that there is not a greater increase over time in the fixation score on the drug day.

SUMMARY OF STUDY I

Six subjects were tested on the spiral after-effect under two conditions on two separate occasions. The two conditions were (i) administration of placebo, (ii) administration of 400 mg. meprobamate. Testing on each day was done once before administration of the treatment and $\frac{1}{2}$, 1, $1\frac{1}{2}$, $\frac{1}{2}$, $2\frac{1}{2}$, 3, $3\frac{1}{2}$, 4, $4\frac{1}{2}$ hours after treatment.

A test of fixation was given before administration of the treatment and $\frac{1}{4}$, $1\frac{3}{4}$, and $3\frac{3}{4}$ hours after administration.

The results showed that the spiral after-effect was decreased after administration of meprobamate and that the results could not be explained in terms of poorer fixation after the treatment.

STUDY II

METHOD

The apparatus used was exactly the same as in Study I.

In this study three expansion trials were given with a one-minute rest pause between trials. The change from one contraction trial, followed by one expansion trial used in Study I, to three expansion trials, was due to the agreement between subjects that the expansion effect was more clearly defined than the contraction effect.

Each subject was given two treatments (1) placebo, (2) 600 mg. meprobamate on two different days, the order of treatments being counter-balanced. Both the placebo and meprobamate were in identically appearing tablet form and taken orally.

On each day the subject was given one session before treatment (initial session) and four sessions 1, $2\frac{1}{2}$, 3, and $4\frac{1}{2}$ hours after administration of the drug or placebo.

The Holland test of fixation was given immediately after each spiral after-effect test at each session.

SUBJECTS

The total N in this study was six. All were female subjects. The ages of the sample ranged between 25 and 45 with a mean of 35.3.

RESULTS

An analysis of variance on the mean after-effect scores at each session did not produce a significant treatment effect. A second analysis of variance was done on the raw scores. Table III shows the results of this analysis of variance. It will be seen that two significant F ratios emerge, namely, those for "Subjects" and "Times". Figure 2 shows the results in diagrammatic form. It can be seen that the results are in the right direction, i.e. the after-effect on the drug day is shorter than on the placebo day. It is noteworthy that as in Study I, the difference between the scores for each day remains constant over time.

That the F ratio for "treatment" is not significant is due to the size of residual 1 against which the "treatment" effect was tested. This residual,

TABLE III

Source				Degree of Freedom	S. Squares	Mean Squares	F	P
Subjects	..	..	..	5	1651.04	330.21	30.05	< .01
Days	..	..	..	1	2.06	2.06	—	N.S.
Treatment	..	..	..	1	36.00	36.00	3.27	N.S.
Residual	..	..	..	4	43.97	10.99		
Total	..	..	..	11	1733.07			
Times	..	..	..	3	46.04	15.35	7.11	< .01
Time-Subject	..	..	..	15	43.80	2.92	—	N.S.
Time/Treatment	..	..	..	3	2.45	.82	—	N.S.
Time/Day	..	..	..	3	7.01	2.34	—	N.S.
Residual	..	..	..	12	25.98	2.16	—	
Total	..	..	..	36	1858.35			
Final residual	..	..	..	96	196.85	2.05		
Total	..	..	..	143	2055.20			

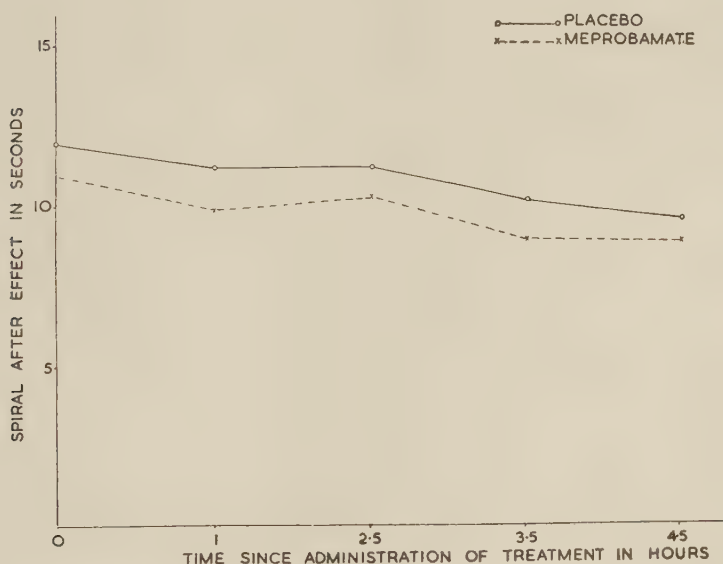


FIG. 2.—Duration of the spiral after-effect in seconds for a group of subjects under drug treatment (Study II).

significantly greater than the other residuals, is due to individual differences in reaction to the treatment. An extensive study into the effect of different dosages of meprobamate is under way and may throw more light on these individual differences and on the absence of a time/treatment interaction.

The possibility that the significant "Time" effect was due to the use of "expansion trials" rather than "contraction" and "expansion trials" was investigated with negative results. The investigation is reported in detail elsewhere (1).

Two product moment correlation coefficients were calculated. One of them was between after-effect scores and fixation scores at the initial session on the first day using data from both Study I and Study II; $r = .075$. The other correlation coefficient was between the same readings on the second day, $r = .065$. The spiral after-effect does not appear to be related to fixation as measured by Holland's test.

SUMMARY OF STUDY II

Six subjects were tested under two conditions each on two separate occasions. The two conditions were (i) administration of placebo, (ii) administration of 600 mg. meprobamate. Testing on each day was done once before administration of the treatment and 1, $2\frac{1}{2}$, $3\frac{1}{2}$ and $4\frac{1}{2}$ hours after administration.

A test of fixation was given at each of the above sessions.

The results showed that (i) there was a significant decrease in the spiral after-effect over time, (ii) the main treatment effect was not significant, owing to individual differences in reaction to the drug, (iii) the spiral after-effect was not correlated with the fixation measure used.

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PSYCHOSES DUE TO AMPHETAMINE CONSUMPTION

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INTRODUCTION

IN spite of the publication of Connell's monograph on amphetamine psychoses in 1958, the frequency of such states does not yet seem to be widely recognized even among psychiatrists. Nor is it fully appreciated in what unexpected settings such psychoses can occur, so that many cases must still be overlooked, masquerading for the most part as examples of paranoid schizophrenia.

Before Connell began collecting the material on which his monograph is based, only three cases of psychosis due to amphetamine had been published in this country and during the progress of his work only three further cases were described. Yet Connell was able to add 42 cases to this scanty literature. The frequency of the condition is again emphasized by the fact that in the past sixteen months, seven cases of amphetamine addiction, each of which has been seen in the Department of Psychological Medicine of the University of Durham, has at some period suffered a psychotic breakdown.

The first examples of psychosis associated with the taking of amphetamine were described by Young and Scoville (1938). Of three cases described, in one only was the psychotic episode definitely attributable to amphetamine. This was a man of thirty-four years taking 40–60 mg. of amphetamine daily for narcolepsy. He believed that he was being poisoned and expressed intense ideas of reference. He improved quickly once the drug was withdrawn. Increasing attention was paid to the condition on the Continent and eleven cases were described in 1954 by Bonhoff and Lewrenz. Many more cases have been reported from the United States of America, notably among prison inmates (Munroe and Drell, 1947).

The pattern of the psychiatric disturbances reported in the literature varies considerably. Cases of delirium are described by Brown (1945) and Delay (1950), acute mania by O'Flanagan and Taylor (1950) and catatonic states by Micheaux (1950) and Abely (1950). The greater number of the reports mention the existence of paranoid features, and in many the illness is described as taking the form of a paranoid psychosis (Herman and Naylor, 1954; Askevöld, 1959). Amongst Connell's cases the pre-eminent features of the psychoses were ideas of reference, paranoid delusions and hallucinatory experiences. Only three patients were disorientated and in two of these other factors existed which may have been responsible for this phenomenon.

Case 1. A male patient aged 35 years whose parents belong to Social Class 1. During adolescence he developed a fetish associated with tension symptoms. In 1941 as a student he began to take "benzedrine", partly to stay awake at night and because he found that it increased his erotic sensations. In 1947 he suffered an attack of gastro-enteritis which persisted for about five weeks and was followed by an acute psychotic episode. He became paranoid and convinced that he had committed a murder which he had seen reported in the newspapers. He heard voices discussing and criticizing him and saw faces which peered at him from behind pillars. He was depressed and agitated and made a suicidal attempt. A diagnosis of paranoid schizophrenia was made and he was given a course of modified insulin. Within a year the same state recurred and he was treated with E.C.T. followed by a course of deep insulin. He continued to obtain amphetamine whilst in hospital and showed wide mood swings and fluctuating psychotic features. He was eventually discharged and remained out of mental hospitals for the next eight years, during which time he drifted from job to job. He then became acutely paranoid, thought he was the victim of an international gang and in 1956 sought mental hospital admission. His condition settled on chlorpromazine. Six months later his paranoid state returned and during the next year he was readmitted to hospital three times. The last of these admissions was prompted by a suicidal attempt with barbiturates. He continued to be aggressively paranoid and early in 1958 a prefrontal leucotomy was performed. On his discharge from hospital he began to take "persomnia"—as well as dexamphetamine—and was readmitted after taking an overdose. He was transferred to another hospital but absconded and was eventually admitted to this Department in August, 1958 after taking an overdose of chlorodyne.

He was quiet and withdrawn with flattened affect and showed a number of paranoid ideas relating to the details of hospital routine. There were no florid psychotic features. Whilst out one afternoon he took an overdose of chlorodyne and "persomnia" and in a subsequent search of his possessions many empty tubes of preludin were found. He admitted that he had taken it persistently for the previous six weeks whilst in hospital. A close watch was kept and during the next few weeks the patient lost his paranoid ideas and his insomnia. He became morose and more solitary and eventually took his own discharge. He has since been admitted to another mental hospital.

Case 2. A male patient aged 39 years belonging to Social Class 3. He was illegitimate and for many years had practised as a passive homosexual. He was invalided from the Army in 1943 on the grounds of psychoneurosis and subsequently took up nursing but failed to qualify. He vacillated between various nursing jobs and spent occasional periods in a Dominican Order. In February, 1953 he began to take methylamphetamine. During 1954 he increased the dosage to 100 mg. a day because of loss of confidence and towards the end of that year began to hear many distant, indistinct voices and felt that he was being followed about by the police. The voices became nearer and more distinct and people started to laugh at him. He was admitted to a mental hospital in April, 1955 where a diagnosis of paranoid schizophrenia was made. He was given a full course of deep insulin therapy. His symptoms ceased within a week of admission, before his first coma. He continued to take methylamphetamine after his discharge and towards the end of 1956 developed ideas of reference concerning his homosexuality. He was admitted to another mental hospital for four months where his symptoms rapidly improved. During 1957 he began taking mist. pot. brom. et chloral in quantities up to 5 ounces daily and by April he was again auditorily hallucinated and was once more admitted to a mental hospital. He heard voices which he recognized, accusing him of various delinquencies and the night after admission he saw "a full coloured film" on the walls of his room and through the window, in which a tremendous conspiracy against him was played out, culminating in the arrival of police cars. He continued to take mist. pot. brom. et chloral after his discharge and soon felt that people were talking about him and spying on him with glasses which could see through walls. His sleep became disturbed by hallucinatory voices which commanded him to go to various places and others which threatened police action. He was readmitted to a mental hospital in November, 1957 for a period of eight weeks. The diagnosis was regarded as schizophrenia and he was treated with E.C.T. and "frenquel". Following his discharge he began to take sodium amylal up to g. 18 daily with a small amount of "drinamyl". He felt tense, with strong feelings of insecurity and was admitted to another hospital where he was given lysergic acid with little effect.

Coming north, he obtained supplies of "drinamyl" from two doctors and was taking about ten tablets daily together with 250 mg. of preludin. He was admitted at the request of a general practitioner, who was alarmed at the quantities of "drinamyl" he was taking in view of his previous history. At this time he showed no psychotic features though he was very tense and anxious.

Case 3. A female patient aged 32 years belonging to Social Class 1. In 1953 for a period of several weeks she took large doses of pethidine following a miscarriage. When the pethidine was discontinued she began to take variable quantities of dexamphetamine and preludin. She had always been quick tempered, easily offended and an inefficient housewife and these character traits became accentuated at this time. In 1954 she showed a variable depression and made a number of threats to attempt suicide. Following the birth of a child she became very excited, restless and sleepless and was mildly disorientated and confused. She felt that her

husband was trying to harm her and attempted to shoot him. She was admitted to a mental hospital but her transfer took several days and by the time she arrived her mental state was normal. Several weeks later it was realized for the first time that she was taking large quantities of drugs, including preludein—up to 50 tablets (1,250 mg.) daily. Her supply remained controlled until July, 1958, when she discovered it was freely available without requiring a prescription. During this period of over three years she was quarrelsome and subject to periods of depression but showed no psychotic features. She increased her intake of preludein and latterly was taking up to 75 tablets (1,875 mg.) daily. She became restless, clumsy and “appeared to do things too quickly”; she was mildly confused and seemed to have “a false idea of time”. She felt that her husband and children were behaving in such a way as to get her into trouble and believed that her husband was trying to get rid of her. She felt that people outside were laughing at her and as a result became unwilling to leave the house. In the dark she saw ill-defined moving shapes “like a mirage” but retained insight into this phenomenon. She lost one stone in weight.

At various times in the past five years she has taken pethidine up to 300 mg. daily when available, alcohol episodically, small quantities of morphine, sodium amytal, which she found to be of no value, and promethazine hydrochloride, which she has taken in doses of 150 mg. as a sedative. Her paranoid features disappeared within a few days of admission to hospital.

Case 4. A male patient of 35 years belonging to Social Class 1. His previous history revealed evidence of psychopathic traits. For three years he had become increasingly aggressive and solitary and was retrospectively jealous of his wife, constantly questioning her about possible infidelities. Latterly he began to indulge in a lot of religious and metaphysical discussion. He admitted to taking dexamphetamine for a period of two years, latterly as much as 250–300 mg. daily.

On admission he appeared very tense. Much of his conversation centred around his search for perfection of a religious nature which he believed could be attained by a spiritual union of man and woman by a process he described variously as “binary fission” and “binary fusion”. He believed that the world was going to end the following day and was convinced that a bearded fellow-patient was John the Baptist. In the presence of this patient his conversation on religious topics became rambling and almost incoherent. There was no clouding of consciousness.

His condition settled and he was allowed out. Once again he developed psychotic symptoms, insisting that people had given him drugs with some evil intent and that the nursing staff was putting “knock-out” drops in his tea. This state settled within 36 hours but for the following five days he was very depressed, lying in bed weeping. Both on admission and during this relapse his urine gave a positive methyl orange test for amphetamine.

This patient was still well a year after his discharge from hospital. The diagnosis of paranoid schizophrenia was considered very seriously in view of the form of his illness, but the clear relation of the psychotic episodes to dexamphetamine consumption left no doubt as to the true nature of the illness.

Case 5. A male patient aged 30 belonging to Social Class 1. During 1955 he began to take dexamphetamine to help him with his studies and shortly afterwards had to take quinalbarbitone for insomnia. During 1956 his work became erratic, he was unpunctual and he would often remain awake all night doing odd things about the house. After some months his behaviour improved and he remained fairly well until June, 1958 when various difficulties led him to increase his intake of drugs. His behaviour became increasingly disturbed. He accused his wife of inefficiency, of hiding his personal possessions, of lying and of stealing from him. During the next five nights he scarcely slept; instead he would wander restlessly about the house, abusing his wife's relatives and crying at times. Occasionally he would destroy books and small articles of furniture or throw them out of a window. He was aggressive to his wife on several occasions. During the day his behaviour was more controlled.

He was seen on the morning of the 5th day. He was restless, unable to sit still and his speech was slurred. At times he talked incoherently and he was unable to give a consecutive account of his illness. He was querulous and insisted that it was his wife who was mentally ill, not himself. There was evident clouding of consciousness. He was admitted to hospital where his mental state returned to normal in two or three days. In his possession were found large quantities of various barbiturate preparations, dexamphetamine and “drinamyl”. He would not admit to taking more than therapeutic doses of these drugs.

Case 6. A female patient aged 19 years belonging to Social Class 4. The general behaviour and work record of this patient were characteristically psychopathic. She was associating with a married man and when her sister, with whom she lived, discovered this fact she was given the choice of breaking the association or leaving home. She had been attending her general practitioner because of tension symptoms with periods of variable depression and had been given a supply of “drinamyl”. Following the squabble with her sister, impulsively she swallowed her entire supply of 50 tablets. Three hours later, on admission to hospital where her stomach was washed out, she was drowsy but there were no abnormal physical signs. Her pupils were normal, her pulse 76 per minute and her blood pressure 130/75 mm. Hg. Two

hours after this she became restless, excited and appeared fearful. For 24 hours she was hyperkinetic, showed some clouding of consciousness with disturbed orientation and was both visually and auditorily hallucinated. The following morning her mental state was normal and she was able to give a clear account of herself.

Case 7. A male patient aged 36 years belonging to Social Class 1. This patient is unique in the series in so far as his psychosis was a withdrawal phenomenon. His addiction was to "desbutal", each capsule of which contains dexamphetamine 5 mg. and pentobarbitone sodium 30 mg., and it may be therefore that it was withdrawal of the barbiturate rather than of the amphetamine which played the major part in provoking his symptoms. He began taking "desbutal" in 1952 and latterly was taking up to 25 capsules daily. He was noted to have become bad tempered and to show mood swings and since 1956 his work had become very erratic. He would sleep at odd times during the day and for periods seemed dazed and would stagger. He decided to stop taking his capsules and three days after became mildly confused, wandered restlessly through the house at night and insisted that there was a stranger in the room with him. He was admitted to hospital after a further three days following a single grand mal convulsion. He was confused, showing disturbed orientation with a degree of confabulation. He was hallucinated, stating that he saw blue fish behind the curtains and in the ward syringes and that there were mice under his bed. This state continued for 48 hours and recurred in diminishing degree during the following six nights. Subsequently his mental state became normal and he has remained well for the past year.

DISCUSSION

It might be expected that the consumption of large quantities of the amphetamine series of drugs would give rise to clouding of consciousness with delirious features, excitement and evidence of overactivity of the sympathetic nervous system. In fact such states do occur, as in Cases 5 and 6, but this is not the common picture. In the majority, the picture resembles more closely that of paranoid schizophrenia and if there is any clouding of consciousness it is of such subtle degree as to remain undisclosed by clinical examination and the use of ancillary methods of investigation. Without knowledge of the drug intake and an accurate picture of the development of the psychosis, it is all too easy to misdiagnose the condition as schizophrenia. This is well exemplified by Case 1, who had been regarded as a schizophrenic for a number of years and who had received courses of E.C.T. and of deep insulin therapy in various hospitals, culminating in a prefrontal leucotomy carried out largely because of disturbed behaviour associated with his auditory hallucinations. We, too, were content at first to accept this diagnosis, though he showed no florid psychotic features, until his large intake of amphetamine and precludin came to light. Another of the series (Case 2) had received a course of deep insulin treatment after a firm diagnosis of schizophrenia had been made, but the correct diagnosis was made during his second episode when he was admitted to another hospital. In other cases, the diagnosis of schizophrenia was strongly suspected or considered, only to be abandoned when the aetiological agent was discovered.

As a rule, once suspected, the diagnosis of amphetamine psychosis is easily confirmed by ensuring that the drug intake ceases. Amphetamine addicts are at least as resourceful as chronic alcoholics and tablets are particularly easy to conceal. Nevertheless, an experienced nursing staff should have no great difficulty in eliminating the possibility of amphetamine consumption once this has been considered. The psychotic symptoms can be expected to disappear within a few days of drug withdrawal, though it is likely that as in other symptomatic psychoses an occasional patient may continue to have symptoms for weeks or even months after the causal agent has been removed. In five of Connell's cases, symptoms persisted for 2-4 weeks and in two for more than 4 weeks after withdrawal of the drug. Persistence of symptoms for many weeks was a feature of two cases described by Chapman (1954).

In the great majority of cases, withdrawal of amphetamine can be carried out without danger. Depression or sleepiness may occur and it is possible that occasionally a psychosis may result. Askeveld (1959) describes four cases in which acute delirious reactions occurred 3–10 days after the withdrawal of amphetamine. Three of these cases were also taking barbiturates and in one, the psychosis was preceded by convulsions. Nevertheless, the author believes that the effective agent was amphetamine. In Case 7 described in this paper, a withdrawal psychosis occurred after a latency of three days, but in view of the coexisting heavy barbiturate consumption, it is difficult to attribute this entirely to amphetamine.

Clinically, the first psychotic episode associated with amphetamine may be difficult to distinguish from a process disorder, but in a long-standing case there are a number of points which suggest the true diagnosis even though the drug intake be denied. Behavioural disturbances of a psychopathic kind are frequently present long before the onset of the illness; the history is often remarkably episodic, the psychotic symptoms generally responding quickly to hospitalization, whatever form of treatment is given. Once the episode has been terminated by withdrawal of the drug, however long the total duration of the illness, it is apparent that there is little or no evidence of personality deterioration. The patient's powers of abstraction are unimpaired, there is no particular paucity of ideas, no limitation of interests, no withdrawal and no autistic features.

The methyl-orange test as modified by Connell (1958), though time consuming, is of value in detecting the presence of amphetamines in the urine and in estimating their amount. It has the disadvantage that other amines also give a positive result. Paper partition chromatography can be used when it is felt necessary to use a test of absolute specificity.

Before the commencement of their drug addiction, evidence of an abnormal personality is common in these patients. In some, the personality disorder appears to be emphasized and aggravated by the amphetamine and grosser disturbances of behaviour may be displayed. This was seen in Cases 3, 4 and 6. A case not described above, as at no time did he show psychotic features, may also be relevant in this context. This was a man of twenty-five years who both as a child and an adult had found great difficulty in making satisfactory interpersonal adjustments. Whilst in the R.A.F. he suffered periods of amnesia and was eventually discharged following a suicidal gesture when arrested for being absent without leave. He began to take up to 24 tablets of dexamphetamine and "drinamyl" daily at the age of 19½ years and shortly afterwards claimed that he felt he was really a woman and occasionally dressed up in female clothing. He persisted in these views for two years and was regarded and treated as a transvestist. When his intake of amphetamine was discovered and curtailed, he proclaimed that the views he had expressed were "a load of rubbish" and since this time his behaviour has been more stable. This patient is so psychopathic and unreliable a witness that too much importance should not be attached to his history. However, the suggestion remains that not only was his psychopathic behaviour aggravated whilst he was taking dexamphetamine but transvestist tendencies were brought to light, fading when the drug intake ceased.

All the cases described in this paper, in fact, showed evidence of a psychopathic personality as defined by Schneider (1950) before they became addicted to amphetamine. This is a common observation in published cases (Herman and Nagler, 1954; Monroe and Drell, 1947), though in two of the cases described by Nandelstadh (1957) it is claimed that there was no evidence of

any previous psychopathic traits. The added disability of recurrent psychotic episodes renders the achievement of such social adaptation of which the patients might be capable much more difficult and is reflected in their work records. This was particularly evident in Cases 1 and 2, whilst in others, Cases 4 and 5, the full realization of their potentialities appears to have been prevented by the drug intake and its consequences. As with other drugs, it seems that amphetamine addiction is likely to arise only in patients of abnormal personality. The factor of opportunity is also evident in this series, five of the patients described having access to the drug through their nursing or medical duties.

Another striking feature is that in many of the cases, excessive quantities of other drugs were also taken from time to time. Varying amounts of barbiturates, preludein, alcohol, potassium bromide, "persomnia", chloral, pethidine, chlorodyne and morphia were taken by different patients and sometimes it appeared almost immaterial what was taken providing the quantity was large enough. In Case 2 a psychotic episode indistinguishable from those occurring earlier as the result of amphetamine, followed the consumption of large quantities of bromide and chloral. Levin (1947) has described thirteen cases of bromide intoxication in which a schizophrenic-like illness resulted. Three patients who encountered difficulties in acquiring sufficient supplies of amphetamine, found a satisfactory substitute in preludein. These three patients have taken large quantities of this drug and in one of them the psychotic episode which occurred appeared to be largely attributable to this agent. The recent literature confirms the increasing frequency of psychotic illnesses due to preludein and in the last two years a number of such cases have been reported in this country (Bethell, 1957; Clein, 1957; Glatt, 1957; Kahan and Mullins, 1958; Silverman, 1959). The psychosis may take the form of a schizophrenic-like illness, or may be accompanied by clouding of consciousness and disorientation. Preludein can still be purchased freely from chemists' shops and it would appear highly desirable that it should be placed on Schedule IV of the Poisons Rules at an early date.

The series of cases described in this paper shows two trends which appear to be typical of amphetamine psychosis. The frequency of the condition is greater in males than in females and, as emphasized by Askevold (1959), the social status of these patients—at any rate before the commencement of the period of addiction—tends to be high. Five of the seven patients described belonged, at least for a period, to the Registrar General's Social Class I.

It is of considerable interest that a euphoriant drug should give rise to a clinical picture so similar to that of schizophrenia. The simplest explanation of this fact would be that an incipient or latent schizophrenia had been brought to light by the amphetamine. The cases described in this and other papers provide little or no support for this view. The course of the illness differs sharply from that of schizophrenia, as has already been emphasized. Furthermore, in the seven cases described, in none could a history be obtained of any schizophrenic relatives. As already noted, in one of our patients a psychotic episode of the same kind was associated with a high dosage of bromide and chloral. Langfeldt (1957) points out that the majority of drugs of addiction may give rise to paranoid reactions, though in this respect amphetamine appears to be particularly potent. In no way can such paranoid states be regarded as specific effects of amphetamine, for, apart from the fact that so many other agents give rise to a similar picture, amphetamine itself may on occasion give rise to other forms of psychosis. Similar schizophrenic-like illnesses may be associated with aetiological agents other than drugs. That an epileptic psychosis

can take a form clinically indistinguishable from schizophrenia is a matter of common observation. Both myxoedema and pernicious anaemia may give rise to paranoid psychoses and the picture of alcoholic hallucinosis (Benedetti, 1952) has many similarities. Some cases of post-operative subacute delirium, in which such clouding of consciousness as may be present has to be inferred, bear a very close resemblance to amphetamine psychosis, and their distinction from schizophrenia is made more on the obvious relationship to the operation and on their favourable outcome than from differences in the clinical picture. Particularly in the case of amphetamine psychosis, it is tempting to view the condition in the light of some of the theories concerning the aetiology of schizophrenia, notably the view of Hoffer and Osmond (1959) that the symptoms result from the products of abnormal adrenaline metabolism. That the same clinical picture results from so many processes suggests that the immediate aetiologies may be related. The paranoid psychosis may be regarded as the expression of a final common path. In the case of schizophrenia, this is activated by a metabolic abnormality dependent in part on genetic structure. It is also capable of activation by many other metabolic disturbances, including the excessive consumption of amphetamine.

SUMMARY

Seven cases are described in which psychotic illnesses occurred in association with amphetamine consumption.

In four of these the diagnosis of schizophrenia had been made or was seriously considered.

In two cases, the psychosis took the form of a delirium and in one a delirium occurred as a withdrawal phenomenon. In this latter case, barbiturates may have played a more important aetiological role than amphetamine.

The differential diagnosis of paranoid psychoses due to amphetamine consumption from schizophrenia is considered.

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A CONTROLLED TRIAL OF HYPOTHERMIA IN CHRONIC SCHIZOPHRENIA

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INTRODUCTION

PHYSICAL methods play an important part in psychiatric treatment. The roles of electroconvulsive therapy and, to a lesser extent, insulin coma therapy, are fairly well-defined and their effectiveness recognized, though different authorities qualify their recognition in various ways.

In searching for a new physical method it is reasonable to look first for a common factor in the therapies which have achieved some success. Insulin coma and its dangerous but effective complication "irreversible" coma, are both associated with the cessation or reduction of higher neuronal activity, or disruption of its organization. Electroconvulsive therapy depends for its effectiveness on the production of an epileptic fit and this results in temporary cessation of cortical signalling activity if electro-encephalographic silence can be so interpreted; Gastaut (1) suggests that the major fit is the outward sign of a rhythmic inhibitory system which produces cortical extinction. If cessation of existing neuronal activity were a common factor it would be sensible to look for other ways in which this could be brought about.

The number of possibilities is limited. Methods such as hypoglycaemia, hypoxia and sedative drugs, though effective in certain types of case, reduce not only the capacity of the neurone to discharge but its ability to maintain its own integrity. It follows that the risk of neuronal death is high if the therapy is vigorously done. It might be possible, by artificially induced specific hypovitaminosis, so to disrupt enzyme systems within the neurone that the cell failed to function but remained viable; neuronal sparing in spite of severe hypofunction in Wernicke's syndrome has been described. To use hypovitaminosis therapeutically would be a very cumbersome procedure.

On the other hand temperature reduction, if carried far enough, would be likely to reduce neuronal activity and at the same time the maintenance metabolic needs of the cell. It would therefore be reversible and unlikely to cause neuronal damage. To suggest hypothermia as a physical treatment is only to echo other workers (2, 3), but in view of the successful introduction of hypothermia into surgery it now seemed reasonable to attempt its psychiatric application. Accordingly it was decided to conduct a controlled trial of this treatment on a small number of patients which, if the results were encouraging, would be expanded later. This paper reports the conduct and results of the pilot scheme.

METHOD

(a) *Selection of Patients*

It was not possible to predict what mental changes, if any, would occur as the result of hypothermia. It was felt that the patients treated should have a wide range of symptomatology and should have failed to respond to previous treatment. Further, their prognosis should be bad and if possible they should be in a steady state as far as the level of their symptoms was concerned. Chronic schizophrenics were thought to be suitable. To reduce risk only physically fit patients under forty-five years of age, free from obesity, chest disease or electrocardiographic abnormality, were selected. Fourteen pairs of patients were matched for age, duration of illness, ward, and, where possible, diagnostic subgroup. The patients were all male and came from Horton or Springfield Hospitals.

Patients came in pairs to Atkinson Morley's Hospital and were assessed, before and after treatment, by interview and psychological testing. One of each pair had an anaesthetic with hypothermia, while the other had an anaesthetic producing the same period of coma but at normal temperature, as described later. The recipient of hypothermia was decided by a randomizing method supplied by Dr. Fairbairn. Successful precautions were taken to arrange that those who assessed the patients did not know which was the experimental subject and which the control.

(b) *Selection of Temperatures*

Reports of cases of accidental hypothermia show that consciousness is lost at 28–30° C. It was decided to cool all the experimental group down to 30° C. and keep them at this temperature for one hour. Surface cooling by means of ice bags was the method adopted.

(c) *Treatment*

Pre-medication. To facilitate accurate assessment it was essential to maintain the patients on any sedative or tranquillizing drugs that they were accustomed to receive. The drug most commonly employed was chlorpromazine. On the day of treatment all drugs were stopped and immediate pre-medication obtained by omnipon gr. 1/3 (20 mg.) and scopolamine gr. 1/150 (0.4 mg.) in the early cases, but later this was changed to pethidine 100 mg. and atropine gr. 1/100 (0.65 mg.).

Anaesthetic Technique. Anaesthesia was induced with a small dose of thiopentone and oral intubation carried out under suxamethonium. Owing to the difficulty of performing venepuncture at low temperatures, an intravenous transfusion of dextrose-saline was set up and all subsequent injections

given into this drip. Maintenance of anaesthesia was achieved by a mixture of oxygen and nitrous oxide in equal proportions, to which ether was added as required. Further muscle relaxation was obtained by the use of d-tubocurarine. Respiration was manually controlled through the treatment, a carbon dioxide absorbing apparatus being included in the anaesthetic circuit.

Hypothermia. Once anaesthesia was established an E.C.G. monitor was set up and an electrode of a thermo-couple placed in the oesophagus to record temperatures. The naso-pharyngeal temperature was registered on an alcohol thermometer lying in the nose. Recordings of pulse rate, blood pressure and temperatures having been noted, the patient was cooled by the application of three plastic pillow cases partially filled with crushed ice. These were placed so that they encircled the patient's trunk. Pulse rate, blood pressure and temperature were recorded at five-minute intervals until a temperature of $31\frac{1}{2}^{\circ}\text{C}$. was reached. The ice was then removed and an after-drop of $1\frac{1}{2}^{\circ}\text{C}$. was usually obtained. It was observed that by this method patients weighing between 9 and 12 stones lost one degree Centigrade every fifteen to twenty minutes.

Re-warming. Patients were re-warmed by means of plastic water blankets, water being pumped through them at 45°C . Warming was continued until a temperature of 35°C . was attained. At this stage patients were allowed to wake up; the young shivered but the elderly and those accustomed to receiving generous doses of chlorpromazine did not do so.

Control Patient. The control series of patients were treated in a like manner to the above except that ice was not applied. The period of anaesthesia was similar to that undergone by the cooled patients.

(d) *Psychological Testing*

The selection of tests had to take into account not only the self-evident criterion of an objective and valid measure of psychoticism (that is, in this context, of chronic schizophrenia) but also tests which would be easily administrable to a group of chronic schizophrenics. These are described in detail below:

(i) *Figure Reconstruction Test.* This test requires the reproduction of geometrical designs from memory, as developed by Brengelmann at the University of London Institute of Psychiatry. The present form represents a level of difficulty well below a mean level and involves a number of different measures, all objectively scored, of error and expressive movement (4).

The reproduced designs are scored for:

(a) Rotation error of the individual shapes around a central reference point. The scores are expressed in degrees. This involves, of course, memory of the placement of the figures.

(b) Distance in millimetres from the centre of the individual shape to a central reference point.

(c) Size which is expressed in 1/10 millimetre. These latter two scores are of expressive movement.

A further addition to the memory portion of the Figure Reconstruction Test is the recognition section. Thirty patterns, ten of which are actually presented in the memory test are assembled on a recognition card. Subjects are asked to give two statements; firstly whether they think they have seen a particular pattern before during the memory test, and secondly how certain they feel about the correctness of their statement. From this three scores are derived:

1. Positive recognition or the number of "Yes" answers, i.e. number of times the subject thinks he has seen the pattern before irrespective of the correctness of the statement. This score is interpreted as over-inclusion.

2. Certainty in response to the task. The subject is made to choose one of four degrees of certainty (+2, +1, -1, -2). Scores are expressed as means per judgment carried to two decimals.

3. Adequacy of certainty. This score is computed by deducting mean certainty for incorrect responses from mean certainty of correct responses. The subject is said to respond adequately when more certain responses are attributed to the correct answers than to the incorrect ones. Limitations of the not yet fully developed scores of this latter have been expressed by the author (4).

(ii) *Picture Recognition Test*. This test consists of two sets of six pictures. Each was presented in a special box as described (7). The pictures represent commonly known objects, e.g. a pair of spectacles, hands, a human figure, etc. (6). Each picture is shown with the following time exposures: two at 1/100 second, two at 1/5 second, two at $\frac{1}{2}$ second, two at 1 second, two at 3 seconds, one at 30 seconds. The score is the number of exposures required for recognition over the entire set of six cards.

(iii) *Epstein Over-Inclusion Test*. This is a paper and pencil test consisting of a list of fifty words. Each of these is followed by six response words from which the subject is asked to select however many he regards as a necessary part of the concept described by the stimulus word. The test was developed by Epstein (8) and additional information has been derived from the work of Payne at the Institute of Psychiatry (9, 10).

Predictions

1. The results of previous experiments give the following norms for a group of acute psychotics on the Figure Reconstruction Test (5):

							<i>Mean</i>
Rotation error	..	..	..	..	..	..	35.1
Size	..	..	..	..	..	..	126.8
Distance	..	..	..	..	..	..	48.3
Positive recognition	..	..	..	..	..	..	63.5
Certainty	..	..	..	..	..	..	152.7
Adequacy	..	..	..	..	..	..	16.9

The mean scores on the above for the present group should all be the same or higher with the exception of adequacy which should be lower, on the pre-treatment trial.

2. The mean score of the Picture Recognition test on an acute psychotic group was 55.8 (6).

The mean scores of the present study should be the same or higher on the pre-treatment trial.

3. The mean score of a group of schizophrenics on the Epstein Test established in a previous study was 51 (10).

The mean score on pre-treatment in this series should be the same or higher.

4. There should be a significant difference between the experimental and control group scores following treatment.

Method

The patients were tested immediately on admission to this hospital and the day after treatment either by the psychologist or by the nursing staff under the psychologist's supervision.

There were three forms of equivalent difficulty of the Figure Reconstruction test (one for practice) which were randomly varied in presentation. Ten cards were presented in each form using a 30-second exposure time.

Two forms of six cards each of the Picture Recognition test were presented also randomly varied.

The Epstein Over-Inclusion test does not have an equivalent form so the same test was given after treatment.

Co-operation of the patients was secured in all but two cases, one being a mental defective prior to the onset of the illness and the other, a paranoid patient, refused the test.

The results were analysed by *t* tests for correlated means in small samples. Twelve pairs of scores were used for the Figure Reconstruction test, eleven pairs for the Picture Recognition test and six pairs for the Epstein Over-Inclusion test.

The means and variance were calculated for the combined groups on the pre-treatment trials giving an *N* of 24 for the Figure Reconstruction test, an *N* of 22 for Picture Recognition test and an *N* of 19 for the Epstein Over-Inclusion test.

INTERVIEW ASSESSMENT

All patients were interviewed on the day before and the day after treatment, each separately by two observers (P.H. and G.W.), who, after an interval of about a month, did further interviews at the hospital of origin. Interviews were designed to suit the requirements of the Wittenborn Scale for rating currently discernible psychopathology, the sections of the scale used being those applicable to schizophrenic patients, viz. 5, 6, 7, and 8. Such items as could not be scored at interview were assessed at the source hospitals before and after treatment (11).

RESULTS

(a) Psychological Testing

1. The mean pre-treatment scores on the Figure Reconstruction test confirm the prediction made with the exception of Certainty, which is lower than the previously established norms (see Table I). Inspection of the scores on this section of the test reveal that two patients out of twenty-four produced strong negative results. The rest were all highly positive and without these two yield a mean of 154.

TABLE I

Tests	Mean	Variance
Figure reconstruction:		
(a) Rotation error	60.13	534.4
(b) Size	135.17	2,842.4
(c) Distance	51.33	97.9
(d) Positive recognition	64.83	1,324.5
(e) Certainty	137.54	4,789.8
(f) Adequacy	5.71	1,057.3
Picture recognition	57.64	182.3
Epstein over-inclusion	47.00	681.6

These results support Brengelmann's findings with the test and show it to be a valid and reliable measure of psychoticism producing predictable results.

2. The second prediction is supported by the results. The mean pre-treatment score is higher than previously established norms (see Table I) and confirm previous findings that this test is a reliable and valid measure of psychoticism.

No difficulty was experienced in administering these tests to a group of chronic psychotics except as above mentioned.

3. The Epstein Over-Inclusion test produces results which do not confirm the third prediction (see Table I). The mean score is lower than that established in previous studies. However, the result is in the direction of previous findings, does not differ significantly from previous results with schizophrenics and is significantly different from the mean score for neurotics of 17 (10).

Some difficulty was experienced in getting the patients to understand the procedure, hence the small number of results achieved for comparison (six pairs) and at the time of administration some doubt was felt as to the reliability of this measure with such severely ill patients. Reliability was therefore calculated for these results. The reliability of 0.79 indicates that despite the subjective impression, this test is a perfectly reliable measure even with chronic groups of schizophrenics.

4. No significant differences between control and experimental groups following treatment were obtained and therefore the fourth prediction is not confirmed.

Three different tests covering a wide range of measurements of psychoticism were used in the present study. All the results are in the direction predicted and reveal the tests to be stable and valid measures of the processes tested. Clear-cut results are obtained with the Figure Reconstruction test and it is particularly noteworthy that the measure of Over-Inclusion on this test (Positive Recognition) is not inconsistent with the Epstein, confirming previous observations that psychotics tend to have disturbances of thinking of this over-inclusive type.

With so wide a range of apparently satisfactory measures, the failure to find any significant differences between the control and experimental groups following treatment, suggests that hypothermia does not effect any alteration in chronic schizophrenics.

(b) *Interview Assessments*

Statistical analysis of the results failed to demonstrate any significant difference between the measured psychopathology of the control and experimental groups.

As is commonly the case, both experimental and control groups improved significantly for their change of surroundings and increase in attention.

(c) *Clinical Impressions*

Interviewers were struck by the correctness of their guesses about which patient had received hypothermia, the basis of their guesses being their impression that the patients who had received hypothermia were more outgoing and warmer in their emotional responses. The anaesthetist independently considered that some alteration took place in the cooled patients, saying that they

were more "aggressive" on waking, "thrashing about" in a way quite distinct from the controls' mode of waking; and that for a few hours they were "more positive", "able to express themselves better", while "their answers changed from monosyllables to sentences".

This kind of change was not measured by the ratings we used. However, a different type of reaction following different treatments might be expected without implying an alteration in basic psychopathology.

DISCUSSION

The experiment ruled out hypothermia, administered on a single occasion, as an immediately applicable form of treatment in chronic schizophrenia. The difficulties experienced in assessing the patients and the alterations in both control and experimental groups while they were being treated and observed do not call for special mention here.

A firm clinical impression of increased warmth and rapport distinct from any alteration in schizophrenic psychopathology, such as hallucinatory phenomena or delusion formation, was obtained. This was, however, fleeting, and the judgment may be contaminated by our having been able to guess correctly which patients had had hypothermia; one patient, not included in the series, received hypothermia three times and displayed the changes mentioned above to a remarkable degree, though the alteration was an improvement. At the time the experiment was planned no clue as to the likely alterations could be obtained, and an illness with a broad spectrum of symptoms was chosen to which a wide range of observations and measures were applied. Further work should include specific assessment of rapport and measures of the amount of spontaneous and induced interest manifested by the patient.

Further trials would be safer if they used either a temperature of, say, 34° C. maintained for a longer period, or if some method of local cooling of the brain or a part of it could be devised. More obvious and perhaps more prolonged changes might occur if patients less set in their psychoses were treated, or if cooling were done several times: repetition is necessary with other physical treatments.

In the first two cases undergoing hypothermia changes occurred in cardiac rhythm attributable to excess vagal tone. Both were cured by the use of atropine given intravenously. It was therefore decided to change the pre-medication to include this drug, and to couple it with pethidine. A further undesirable effect was observed in those patients accustomed to receiving large doses of chlorpromazine over a long period. At temperatures between 32° C. and 30° C. periods of circulatory failure occurred and in one case (not included in the series) it became necessary to warm the patient up without completing the treatment. Therefore it is recommended that in any future series the patients should be taken off chlorpromazine some time before undergoing hypothermia. Clearly, it would be unwise to attempt any experiment of this kind without the constant presence of the appropriate specialists and their equipment.

SUMMARY

As part of an attempt to assess the effects of hypothermia on psychiatric patients, a group of chronic schizophrenics, divided into control and experimental groups, were appropriately treated and assessed by clinical interview and psychological testing. No significant differences, in the symptoms and signs measured, emerged. Clinical impressions of alterations are described and their implications mentioned.

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TOXIC AMBLYOPIA FROM PERPHENAZINE (FENTAZIN)

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SINCE the introduction of chlorpromazine with its troublesome side-effects, jaundice, leucopenia, agranulocytosis, photosensitivity, etc., the search for safer and more therapeutically effective tranquillizers has continued unabated. Variations of the phenothiazine derivatives based on the promazine ring have been continually introduced with the aim of increased effectiveness together with greater safety.

One of the most recent of these is perphenazine (Fentazin), which the manufacturers claim to be five times as active as chlorpromazine when administered orally to human beings. They claim that when given in the suggested dosage, side-effects are virtually absent. The following account is given of a single case in which an unusual toxic state occurred. So far as is known, no previous case has been reported in the literature as the result of administering any member of the tranquillizer group of drugs.

CASE REPORT

The patient, a boy, aged 16 on admission to a mental deficiency hospital in July, 1956, had been educated at various special schools in Bristol. On admission he had an I.Q. of 57 on Wechsler Bellevue Form I and was a very immature personality. He had a police record for housebreaking and theft. He came from a poor home and lacked parental control.

In an effort to train him in his attitude towards work, timekeeping and social co-operation, he was employed from May, 1958 in the hospital training unit under regular supervision of the clinical psychologist. He adjusted to this situation quite well for about 6 months when it was noticed that his time-keeping deteriorated over about 2 weeks.

On 19 November, 1958 his behaviour became odd. He blacked his face in preparation for the fancy dress dance which was not due until January, 1959. Next day he had become irrational, deluded and auditorily hallucinated. His affect was incongruous. He presented as a case of schizophrenia of acute onset.

He had lost a stone in weight in the preceding two weeks.

As no evidence of spontaneous remission occurred and his behaviour continued extremely disturbed and disturbing to others, it was decided to treat him with perphenazine. No evidence of a toxic state existed on physical examination. Hb. 94 per cent. and W.B.C. were within normal limits.

22.11.58. Fentazin 5 mg. by intramuscular injection and repeated after 6 hours.

23.11.58. Fentazin 8 mg. oral, q.i.d. (total 32 mg.).

The patient became much more settled and quieter but still retained his delusional state.

25.11.58. Fentazin reduced to 4 mg. oral q.i.d. as the patient was now quiet, and Parkinsonian symptoms, drooling and spasticity had developed.

26.11.58. The patient was again more disturbed and gr. 1 sod. amyltal was given with each dose of Fentazin. Aneurine and nicotinic acid were also given.

27.11.58. When being helped to the toilet it was observed that he had to be guided past furniture and other obstructions. It was then realized he was blind.

Neurological examination. Pupils equal and reacted to light. Corneal reflex present. Blink reflex absent. Accentuated reflexes, tremor and rigidity. Fundi normal. Anaesthesia to pin prick above the abdomen. The possibility of a space-occupying lesion or other cerebral catastrophe prompted lumbar puncture.

Blood. Hb. and W.B.C.s normal.

C.S.F. Pressure increased—no block. Clear fluid.

Protein and sugar normal. W.R. negative. Lange 1100000000.

All treatment was discontinued.

The following day, 28.11.58, no neurological signs remained. The patient was able to recognize objects.

E.E.G. on 2.12.58—no specific abnormality.

Chest and skull X-rays 9.12.48—normal.

The patient, by 3.12.58, was rational and co-operative although reserved and cautious in discussing his psychotic symptoms.

On 3.1.59 he was again hallucinated. He was then transferred to the local mental hospital where facilities for deep insulin coma treatment exist.

DISCUSSION

There appears little doubt that this case, while demonstrating the efficiency and potency of the drug, also illustrates one of the problems of using tranquillizers on mentally defective patients. There would appear to be little doubt that perphenazine was an important factor in producing the blindness. What other factors were involved, it is impossible to say. Scott (6) groups quinine, certain organic arsenicals, *felix mas*, salicylates, ergot, aniline, and nitrobenzole together as agents which produce an exogenic amblyopia of sudden onset and recovery, as distinct from the slower process caused by tobacco, alcohol and lead. The relation to general health and to the role of the vitamin B complex has been considered by Carroll (2), and this case shows evidence of a general metabolic upset in the marked weight loss at the onset of the psychosis. The importance of the B vitamins in brain metabolism is well recognized in transamination processes and the pyruvate metabolism. Although the nature of C.N.S. transmission is unknown, acetylcholine, nor-adrenaline, adrenaline and serotonin are all present in varying concentrations in various parts of the brain and it has been suggested that phenothiazines act by blocking the local action of nor-adrenaline. This could also conceivably be the mechanism of a vision defect in the same way as atropine would cause local blockage of nor-adrenaline. Why it should occur in this case and not in others is unknown, although Parkinsonian states are well recognized and a Parkinsonian-like syndrome with upward rolling of the eyes has been noted during the trials of perphenazine in America in 10 out of 12,897 cases (1).

Vogt (7) in discussing the pharmacology of tranquillizing drugs discusses three possible sites of action of chlorpromazine and makes reference to much recent neuropsychopharmacology.

The rapid and profound development of a Parkinsonian state in this case is in keeping with Schulsinger and Jensen's (5) findings. Comparing perphenazine with chlorpromazine they found the most important side-effect to be Parkinsonism in 11 out of 28 cases treated with perphenazine. The dosage level at which it occurred varied from 16 mg. daily to 96 mg. daily.

It has been suggested that mental defectives are mainly composed of a group of individuals with damaged brains, if not physically, then biochemically and that therefore the effects of toxic agents such as the phenothiazines are likely to be more extensive and profound than in the normal brain. In a survey of many of the recent papers and reviews of the use of the promazine group of drugs in the defective no writer has suggested that there is a greater incidence of side-effects in the defective than in the mental hospital patient. However, it could be argued that the schizophrenic brain although not overtly organically damaged is biochemically damaged. Rudy, Himwich and Rinaldi (4) in a survey of the action of several tranquillizers on one group of mental defectives stress the importance of very careful adjustment of dosage and point out overdosage can accentuate, in a brain-damaged patient, latent or compensated neurological defects, and increase the incidence of epileptic fits. Faure, Faure, Fournier

and Eppe (3) stress the extreme sensitivity of mentally defective children to levomepromazine (7044 RP.).

SUMMARY

A case of toxic amblyopia due to perphenazine (Fentazin) in a mental defective patient developing an acute schizophrenic illness is presented. A possible cause and the relation to Parkinsonian states is discussed.

The possible abnormal sensitivity to drugs by mental defective patients and the need for cautious dosage levels is stressed.

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A SURVEY OF 200 WOMEN DISCHARGED FROM A MENTAL DEFICIENCY HOSPITAL

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INTRODUCTION

THE purpose of this survey was to assess the abilities and present status of all the adult women classed as feeble-minded who have been discharged from the Fountain Hospital. This paper is not a comprehensive assessment, but a survey of these patients' past history, together with an interim report on their rehabilitation. In the majority of cases, the present whereabouts and occupation are known by the social worker and have been re-checked over the past eighteen months in the course of normal follow-up contacts.

PREVIOUS STUDIES

A large number of follow-up studies of patients, certified as feeble-minded or having left educationally subnormal schools, have been carried out. Tizard (1958) mentions five reviews in "Longitudinal and follow-up studies" and gives a résumé of 25 further studies in *Mental Deficiency, the Changing Outlook*, edited by Clarke and Clarke. The success rates vary from 36 per cent. in Town's 1931 study to 88 per cent. in Haskell and Strauss' 1943 study. This considerable variation is not surprising, as the groups, as well as the after-care and the criteria of success, differ widely.

O'Connor and Tizard (1956) conclude in *The Social Problem of Mental Deficiency*, after quoting Charles's 1953 paper, that his "study and the many others of its kind fully bear out the statement made earlier that it is quite false to think of feeble-mindedness as something fixed and incurable. It is, rather, an administrative concept and as such is related to the conditions and facilities available in the community."

DESCRIPTION OF THE PATIENTS

The Fountain is primarily a hospital for mentally defective children, but there are 80 beds for feeble-minded and imbecile women at the South Side Home at Streatham. (This hostel is described in Hilliard, 1954.) The present survey of 200 women deals with all those adults classed as feeble-minded who have been discharged from this hospital. All the patients had been certified under the Mental Deficiency Acts (Section 6, 8 or 9) except 23 who had been admitted as "place-of-safety" cases (Section 15) or under Circular 5/52 (Short-term Care). The dividing line between feeble-minded and imbecile is, in some instances, very difficult to draw. In the present survey, the division has been made mainly on the basis of the intelligence quotient, those with an I.Q. above 50 being labelled feeble-minded. The 200 discharged women form about 70 per cent. of the total number admitted with an I.Q. over 50.

Of the 200 direct discharges from this hospital, 30 were direct admissions, the remainder came from other institutions. Many of the latter group were

described as "working patients" regarded as being able to do a certain amount of simple work within the hospital, but their previous institutions did not consider them suitable for licence. The first of the 200 patients was discharged in 1922 and the last in February, 1958; only 8 were discharged before 1946 when there was a policy change and rehabilitation became one of the main aims. Some of the main data concerning these patients is given below:

	Average	Range
Age of entering a mental deficiency institution ..	22 years	2-71 years
Time spent in mental deficiency institution ..	13 years	<1-38 years
Age at discharge	35 years	17-65 years
Number of years discharged (at June, 1958) ..	5 years	<1-36 years

	Percentage
Entered a mental deficiency institution 14 years or under ..	6.5
Entered a mental deficiency institution 15-26 years of age	70
Entered a mental deficiency institution 27 years or over ..	23.5

The intelligence of the discharged group is as follows. One hundred and twenty-three of the 200 have been given a Wechsler Bellevue test, the average I.Q. is 84.1 with a range of 52-113. Twenty-two others were given the verbal scale only of the Wechsler Bellevue test. These 145 are shown in Figure 1.

TABLE I
Intelligence Test Results of Discharged Patients

Test	No. Given	Mean I.Q.	Range of I.Q.
Wechsler-Bellevue	123	84.1	52-113
Raven's Progressive Matrices	128	83.7	59-111
Terman and Merrill revision of the Stanford Binet	117	65.0	40-93

It will be seen that, of these 145 patients labelled and certified as feeble-minded, only 11 per cent. do in fact fall within this category when it is defined with respect to intelligence, i.e. an I.Q. between 50-70.

The results of the other tests are given below. Direct comparison is difficult because individuals had different combinations of tests. Omissions may have been due to the unsuitability of the test, to specific handicaps of the patient, or to lack of time on the part of the psychologist.

One hundred and seventy-six out of the 200 have a score on one or more of these tests, 78 have a score on all three. There are wide divergencies between one person's score on the three tests, as described by Mundy and Maxwell (1958), who discuss the reasons and provide a correction factor. There are also considerable differences from one time of testing to another. The majority show upward rises. The tests were administered by four psychologists, the majority by Mrs. L. Mundy, who also gave these women therapeutic and remedial help. Rises in I.Q. have been shown both after coming into an institution from a bad home background (Clarke and Clarke, 1954), and on going from the institution to a post outside (Mundy, 1957). On the other hand, preliminary comparisons between the Wechsler-Bellevue scale and the new and better standardized Wechsler Adult Intelligence Scale indicate that the former test gives higher scores in the older age ranges by allowing more for deterioration. The 123 who have scores on the whole of the Wechsler-Bellevue test have an

average verbal I.Q. of 81.5 and an average performance I.Q. 8 points higher, 89.7. It will be shown later that the majority have not had a normal upbringing or schooling. The whole problem of the use and meaning of intelligence tests with women who have had so many early adverse influences is a complicated one and has been discussed by Clarke and Clarke. As Jones (1946) wrote, "It may be useful to repeat once more the generally acknowledged fact that the validity of mental tests diminishes when we apply them to groups deviating in cultural norms from the original standardization group."

It does seem that this group are brighter on average than those found in other institutions. However, there is probably a considerable degree of overlap. O'Connor and Tizard (1954) found that the average I.Q. of a representative group of adult institutional feeble-minded persons was just over 73, using the Progressive Matrices test. They also found that two-thirds of the adult institutional feeble-minded had I.Q.s between 60-80.

PAST HISTORY

The handicaps listed below are those which were found most frequently. It is realized that some patients might have more serious handicaps than those mentioned, and that the fact that their mother had died or deserted them when they were young would not be the same handicap for different children. An "average" case history is given in Appendix I. The handicaps can be divided into physical ones such as deafness, eye defects, epilepsy, etc., and social and emotional handicaps such as illegitimacy and death or mental illness of parents. In thirteen cases there are only a few details in the social history from which to assess the handicaps, in a further few cases specific facts were not known, so that in the tables below, the number in each group is given, together with the percentage this represents of the total group in which this fact is known*. In Table II six had both a sight, hearing or speech defect and another physical handicap.

TABLE II

Physical Handicaps					No.	Total	Per-centage
Sight, hearing or speech defects	..	..	..	..	51	190	27
Other physical handicaps	..	..	..	..	26	186	14
Total with a physical handicap	..	..	..	..	71	190	37

(a) *Physical Handicaps*

These handicaps are taken from the heading "physical defects" on the case papers which are completed by the Medical Officer. The "other defects" include epilepsy, endocrine disturbances and any loss of use of limbs. In some of the older cases these defects are not well documented. It will be seen that about a quarter of the group have a sight, hearing or speech defect. This would tend to be a handicap educationally. Not included in the total of 37 per cent. with a physical handicap are the large number with non-specific aches and pains.

* Data from case notes from Fountain Hospital and previous hospitals and from files of L.C.C. Mental Deficiency Departments.

TABLE III

Social and Emotional Handicaps	No.	Total	Per-centage
Illegitimate	45	187	24
Mother or father died or abandoned child before 5 years of age	63	187	34
Not brought up by own parents from 0-10	101	187	54
Brought up in an institution	72	187	39
<i>Total with one or more of the above handicaps</i> ..	114	187	61
A parent, or parent substitute, psychotic, emotionally unstable or in a mental hospital	62	187	33
A parent described as dull or defective	31	187	17
<i>Total parents alive but with a handicap</i>	78	187	42
Mother or father died or abandoned child between 10 and 21	37	190	19
<i>Total with one of the above handicaps</i>	167	191	87
Stated to be emotionally unstable on admission	150	189	79
Has been in mental hospital	19	187	10
Has sibling described as defective or mentally ill ..	40	186	22
<i>Total with one of the above handicaps</i>	192	192	100

(b) *Illegitimacy*

Forty-five (24 per cent.) of this group are illegitimate. This is a much higher figure than that for the children admitted to this mental deficiency hospital. Hilliard and Kirman (1957) write that in a series of 350 admissions to this hospital, twenty-five (or 7.1 per cent.) were illegitimate. The rate for the general population is now about 5 per cent., varying from district to district, but considerably lower than the 24 per cent. found in these discharged adult patients.

(c) *Upbringing*

In the majority of cases, the previous home life of the 200 women was disturbed. Only 13 had lived with their own two normal parents until they were 21. They appear to have had a very high proportion of defective and mentally disturbed siblings; 40 (or 22 per cent.) are mentioned in the social worker's notes. This may arise from a number of factors, and is partly due to the fact that this is a selected group. Families who already have one difficult member are more likely to ask for institutional care, and in some cases when they came from very adverse homes, the same disadvantages are acting on all the family. There are four pairs of sisters in the present 200 and they are all managing their lives in the community, so that in eight cases at least the "defective sibling" is quite capable of earning her own living.

Seventeen per cent. of the parents are mentioned as dull or defective. In some cases these statements are in old notes where immorality and poverty are sometimes used synonymously with deficiency.

Kirman, in Hilliard and Kirman (1957), writes that a child of borderline intelligence is much more likely to be classified as mentally defective if his environmental circumstances are unfavourable. This is equally true of the

adolescent to early twenties group. The term "emotional disturbance" is used widely and covers a variety of very different conditions. This is discussed later under the heading of personality.

(d) *Schooling*

The methods by which members of this group have been fitted into or excluded from the educational system differ both from one county to another as well as from one time to another. The type of schooling that these women had is given below, together with their Wechsler full scale I.Q. where this is available.

TABLE IV

School	No.	Per-centage	No. Tested	Mean I.Q.
Elementary school	58	29	39	88.4
Mixed elementary and special school	34	17	22	81.4
Elementary and not known	7	3.5	5	79.2
Private school or convent	8	4	4	86.3
Special school	39	19.5	22	83.6
Special school and not known	6	3	6	86.6
Special school and institution	4	2	3	63.3
Excluded from special school	3	1.5	2	61.5
M.D. institution only	14	7	8	83.1
No schooling or less than 1 year	2	1	0	—
Not known	25	12.5	12	85.5
Total	200			

Thus 99 or over half the known cases spent some time in an elementary school. Any changes that occurred from one type of schooling to another, where both were known, were always from Elementary (Primary) to Special School and from Special School to Institution.

(e) *Work Before Certification*

Over half of the known cases worked before they were certified. The figures are given below:

TABLE V
Occupation Before Certification

Type of Work	Number
Domestic work	52
Factory work	12
Laundry work	5
Mixed Domestic/Factory/Laundry	13
Other (shop assistant, farm worker, etc.)	13
Large number of varied posts	13
Total	108
Not worked before came to institution	67
Not known	25

(f) *In Prison or on Probation—prior to certification*

Twenty-seven, or 14 per cent. were put on probation, were remanded, or had been to prison before they were certified. The most common offence was

theft. In some cases such small items were involved that it seems likely that the incident was only one aspect of a difficult situation and was used to bring the woman before some authority.

(g) *Cause of Certification*

It is often very difficult to see why a particular girl has been dealt with under the Mental Deficiency Act rather than by such methods as probation, hostel placement, or fostering. Of these 200, 25 per cent. were certified mainly because of their having an illegitimate child, together with, in most cases, no stable home. It seems probable that it was the density of problems in this group rather than any particular single cause that led them to be certified. All the women had at least one of the handicaps listed in Tables II and III, and all but 30 had more than one. Educational backwardness certainly helped to mask their intellectual capacity, but above all there was no one in the community willing to take responsibility for them in their late teens and early twenties.

(h) *In Hospital*

As stated previously, 130 women came from other mental deficiency institutions where they had spent an average of 10·8 years. Whilst in hospital their main occupations had been domestic work, laundry work or sewing. Very little specific training for work outside the hospital or remedial teaching was attempted before their admission to this hospital. Since their admission, it has been limited, being in the main informal and dealing with such matters as personal hygiene and correction of anti-social manners.

(i) *Personality*

Aspects of personality are extremely difficult to describe in a quantitative way. Whatever the method of assessment, the general picture is consistent. The majority of this group were certified in adolescence because they had a type of personality which gave rise to difficulties and no relatives who would be responsible for them. Backwardness and deficiency were of almost secondary importance. From case notes and certificates it becomes obvious that the disturbance in personality rather than the lack of intelligence was giving rise to the most pressing problems.

Various diagnoses and descriptions are given in the notes. The most frequent comment is that the girl has a very bad temper. This is probably part of the general picture of immaturity in adolescence accompanied by emotional instability. A number of girls were noted to be dishonest, and a further group were said to have immoral tendencies. The diagnosis of depression appears to be a broad one, varying from a dull flattening of affect which might be the result of institutional upbringing, to a serious depressive illness.

The patient's personality is usually described on admission and the following table is taken from these descriptions and the reports of the social worker before admission. With such a variety of writers (doctors, social workers, ward sisters) it is extremely unlikely that there is much consistency in the terms used. The patients may have been depicted as rather less favourable than they were to secure admission, but it is interesting that, if this occurred, it was personality defects rather than lack of intelligence that were stressed. A number were described as having more than one personality defect.

TABLE VI
Description of Patients' Personality on Admission

Personality Description	Number	Per-centage
Bad-tempered	45	
Emotionally unstable	43	
Depressive	31	
Moody, obstinate, sullen, slovenly, apathetic	26	
Immature	21	
Hysterical	20	
Paranoid, deluded	13	
Schizophrenic, schizoid	13	
Beyond control	8	
Inhibited, lacking in self-confidence	7	
Obsessed	4	
Aggressive	3	
Psychotic	1	
Total described as one of the above	150	75.0
Dishonest, or before the courts for stealing	20	
Immoral, or having an illegitimate child	36	
Total described only as dishonest or immoral	25	12.5
Total described as any one of the above	175	87.5
No personality defect noted, or stated as pleasant	14	7.0
Not known	11	5.5

The group of 14 where no personality defect is specifically mentioned nor were they described as immoral or dishonest have their main reason for certification given below:

Low intelligence, I.Q. below 76, and no one willing to care for patient	9
Immediate relatives very disturbed	3
Leaving special school and no home	2
	14

This means that, apart from these 14 where no personality defect is noted, most of the traced remainder of the group are described as having a defect in their personality. Some of these descriptions are true of many children and adults and would not be remarked on, if it was not for their high incidence and that in spite of looseness of definition they do appear to have some predictive value as described later.

(j) Licence

One hundred and fifty-three women worked on licence from the hospital before their discharge, and were on licence for an average of $2\frac{1}{2}$ years. They had an average of 2.3 jobs each. Seventy-six had only one post and 32 had two; one woman had 12 and one 10. The remaining 43 had between 3 and 8 changes. The reasons why a particular girl changes her post, or is found unsuitable, are very complex. Employers of mental defectives vary considerably, so that, when a patient is returned as unsatisfactory, it is not always her fault. In the

main, however, employers are carefully selected and give the patient considerable help, sympathy and understanding. This is borne out by the fact that half of those going out on licence had no change of employment and many are still with the same employer now they are discharged. Of the remaining half who had from 1 to 11 changes, the reasons, as far as they could be ascertained, are given below with percentage figures for 193 changes of employment.

TABLE VII
Reason Given for Patient's Change of Employment on Licence

Reason Given	Number	Percentage
Unsatisfactory work or behaviour	65	33
Patient's request	25	13
Patient's health	22	11.5
Change of circumstance in employer	16	8
Absconded	10	5
Unsuitability of employer or post	9	5
Relatives moving or at relative's request	5	3
Patient unsettled at work	2	1
Suspected theft	1	0.5
Reason not recorded	38	20

The type of work done whilst on licence is given below. Several patients did more than one type of work.

TABLE VIII
Type of Occupation Whilst on Licence

Work on Licence	No. of Patients Who did this Type of Work
Hospital domestic	88
Other domestic work	90
Factory	18
Laundry	18
Other	8

Hospital domestic work was preferred for a number of reasons. The rates of pay are fixed on a National Scale and are relatively high; board and lodgings are provided and usually a uniform is worn. This means that the basic difficulties in life are dealt with. There is also companionship, which can be a major consideration for those who have spent many years in an institution. Being the only domestic worker for a family can be extremely lonely. Domestic work in a hospital is also more repetitive than it is in a private house. In a household where only one domestic help is kept, it is difficult for a deprived girl to fit into the family. However, in a number of cases this arrangement has been most successful and each case must be decided individually.

The heading "Other domestic work" includes, besides this family domestic work, routine domestic work in canteens, factories and laundries. Seventy-four per cent. of the women are doing the same kind of work (i.e. hospital domestic, other domestic, factory or laundry work) as they did on licence. The remaining 47 were either discharged without a period on licence or went, on licence, to relatives instead of to a residential job.

DISCHARGED

Only 2 of the 171 patients whose whereabouts are known have been re-certified. One of these went to another institution and has since been discharged, and the other is now working on daily licence from our new hostel for working girls. Contact has been maintained with 171 of the 200, four of these have since died, leaving 167.

The 29 cases whose addresses are not known at present will be discussed first. Twelve of those whose whereabouts are at present unknown, left before a social worker was appointed, and two more were place-of-safety cases and so not here long enough for much contact to be made. Many of the remainder have been followed up for a number of years and it would be known in most cases if they were not managing in the community. There is no fixed follow-up policy; those discharged are encouraged to keep in contact, but there is no pressure to do so. Contact is maintained mainly through a summer party, Christmas letters and by the social worker's help in getting them new accommodation and work when this is needed. Suitable accommodation is one of the main problems, as these patients lack relatives who are willing to give them a home, and lodgings are difficult to find.

None of the former patients whose present address and occupation are known, are in other mental deficiency hospitals, in prison or on probation. Since discharge, three have been "in trouble with the police" but have not been sent to prison. None have been before the courts for prostitution. It is unlikely that any of this group are earning their living in this way, although 7 have had illegitimate children since discharge.

About 20 have returned at some time to the South Side Home, usually for less than a fortnight. It is possible that some of these could be classed as temporary "failures" in that they had nowhere suitable to go, or no work; others were just coming back to the hostel for a night's lodging before going on holiday. Two are at present admitted informally; one has retained her former work and goes to it daily, and the other works in the hospital laundry.

The present living arrangements of the discharged women are given, together with the figures in each group and the number who have been tested, with their average Wechsler Full Scale I.Q. and range, where this is available (123 cases). An additional 22 Wechsler Verbal Scale I.Q.s have been added in both Tables IX and X.

TABLE IX
Present Living Arrangements

Category	Number	Number Tested	Average I.Q.	Range of I.Q.
Living independently	62	48	86	68-108
In a resident post	57	45	80	54-113
With relatives or dependent	48	39	79	52-102
Lost and dead	33	13	89	67-100

The social worker and psychologist placed each woman into one of three categories. The first category comprises those who are completely independent, that is, living in her own house or lodgings, on her own, with another woman or with her husband. The second category includes those in a more sheltered environment, such as that of a resident domestic or hospital domestic. This group are living as independent a life as many other people, but the difficult problems of board and lodging are dealt with. The third category comprises all

those who are living with parents or relatives or are dependent on them. Here in addition to board and lodging being provided, probably someone is present who feels responsible for them and who can give advice. There are some women in both the second and third categories who would be quite capable of running a home of their own and living independently. The three women (one certified and two admitted on an informal and temporary basis) who are living in hostels attached to the Fountain are included in the third category.

PRESENT EMPLOYMENT

Of the 167 individuals traced and alive, 114 are working gainfully, 6 are retired, and 17 (10 per cent.) are not working. The figures in each occupation are given in Table X together with the number tested and their average I.Q. and range.

TABLE X
Employment, Occupation and Intelligence

Type of Work	Number	Number Tested	Average I.Q.	Range of I.Q.
Private domestic work and housewives	71	56	82	62-99
Hospital domestic	42	29	81	54-113
Factory	17	16	87	78-108
Laundry	9	9	87	59-102
Other	5	3	87	70-108
Total working	144	113	83	46-113
At home with relatives or friends ..	9	8	80	64-100
Attending occupation centres ..	4	4	56	52-63
Mental hospitals	3	2	67	52-81
At South Side Home	1	1	85	—
Total not employed	17	15	72	52-100
Retired	6	4	83	73-101
Not traced	29	10	92	80-100
Dead	4	3	78	67-88
Total number	200	145	82.5	52-113

The women who are not working have either an I.Q. below 64, or are very emotionally disturbed. They differ from those working in the length of time they have spent in institutions; this is either less than a year or over 25 years. It appears that this group comprises both the very "institutionalized" woman and those whose relatives merely wanted temporary relief. Those who have retired, have not been traced, or have died, are also shown in Table X. It will be seen that the women who are untraced tend to be brighter than the rest and contain no very dull members. The deaths were due in one case to a kidney disease in a young girl and the remaining three cases to illnesses associated with old age.

MARRIAGES AND CHILDREN

Forty-six out of those discharged are married, about a third go out to work as well as looking after their homes. It is hoped that the married group will be described in more detail in a later paper. Thirty-one of these married women have had children; 70 of these discharged patients have had 160

children. These include most of the children studied in an earlier survey (Brandon, 1957). Their average intelligence level was then found to be within normal limits. Since discharge, seven of the unmarried women have had children.

EFFECTIVENESS OF REHABILITATION

The majority of these discharged women, in spite of a wide diversity of problems, are living and working outside the Fountain. The hospital has always been willing to take back any of these discharged patients if they were in any difficulty, although the first aim was to help them to remain in the community. One can hardly compare groups of successful and unsuccessful patients when the latter contains only 3 subjects. One of these returned from a mental hospital to be nearer her home, another's lodging arrangements broke down, but she retained her work, and a third is very emotionally unbalanced. The only factor all three have in common is that they all have relatives who take a sporadic interest in them rather than no relatives. The patients have been divided by the author into four groups. Group I includes those who are successful in their work and personal relations at home or in their lodgings; these patients do not need help in finding either work or lodgings and it is thought that even if they lose either, they will not need help in the future. Group II may need help with either work or living accommodation, although they have managed or might be expected to manage either one or the other. Group III are managing in the present circumstances, but if their parents died, or the special post which suits them was not available, some help with both work or occupation and living accommodation will probably be needed to keep them in the community. These women are more likely to need hostel accommodation at some time in their lives. Group IV contains the "lost", "don't know", and dead cases. The majority of lost cases probably belong in the most successful category; a number are known to be working although not enough is known about them to place them under any of the "known" headings.

TABLE XI

		No.	Per- centage
Group I	Most successful and need least help	123	61.5
Group II	Might need help with either work or accommodation	17	8.5
Group III	Might need help with both work and accommodation	29	14.5
Group IV	Lost and not known, and dead cases	31	15.5

Thus 46 (Groups II and III) out of 169 (or 27 per cent.), may need help from the Fountain Hospital's social worker or the community social services when and if the present arrangements cease. These figures are only a rough estimate and might vary with the national level of unemployment, but it is probably true to say that only a third required more than friendly interest after the first few years.

PERSONALITY AND SOCIAL ADEQUACY

It was hoped that some useful predictive knowledge might be gained by comparing the personality descriptions given to Group I on entering an institution with those in Groups II and III.

TABLE XII

Personality Description	Group I	Group II and III	Percentage Frequency in Group II and III
A. Social Defects:			
Immoral	26	4	13
Beyond control	5	1	16
Bad-tempered	27	7	21
Dishonest	11	3	21
B. Other Defects or No Defects:			
No defect mentioned	10	3	23
Immature	13	5	28
Emotionally unstable	28	11	28
Moody, obstinate, sullen, slovenly, apathetic	15	6	29
Aggressive	2	1	33
Personality not known	4	2	33
Inhibited	4	3	43
C. Psychiatric Defects:			
Paranoid	5	4	44
Depressive	15	13	46
Hysterical	9	8	47
Schizophrenic or schizoid	5	6	55
Obsessional	1	3	75
Psychotic (1 in Group IV)	0	0	0
Total number of descriptions	180	80	Mean 31

These terms taken from the case sheets and given in Table VI are often lay descriptions and should not be taken as a professional diagnosis. However, when they are arranged in order of the frequency in which they are found, in Groups II and III (the less successful groups) it appears that there is a continuum leading from a group with social defects of personality, through a mixed group to those with psychiatric defects. Those women described as having a psychiatric defect appear significantly more often in Groups II and III ($\chi^2=9.1$, $p < 0.01$). The numbers given in Table XII refer to the number of times a term is used. The χ^2 however is worked out on the number of women who were or were not described as having a psychiatric syndrome. There is also a tendency which is just below the 0.05 level of significance for those who are described as having a social defect to be found more often in Group I (the more successful group) $\chi^2=3.72$.

It appears from the value of χ^2 and the percentage frequencies that women who are described on admission as having social defects of the kind enumerated in Table XII under A have a rather better prediction of future success or complete independence than those who are described as having psychiatric symptoms. It should be pointed out that the whole concept of "more" or "less" successful is only tentative and that, had those with psychiatric symptoms gone to a mental hospital, the outcome might have been different.

Intelligence is obviously of importance in individual cases, but in this survey those with an I.Q. over 80 are not found any more frequently among the more successful ($\chi^2=0.47$), and there is no proved relationship between higher intelligence and psychiatric traits in these patients. The distribution of intelligence is shown in Table XIII.

TABLE XIII
Distribution of Intelligence

	I.Q.				80 plus	50-79	I.Q. Not Known	Total
Group I	..	..	..	..	60	31	32	123
Group II and III	..	..	..	..	25	18	3	46
Group IV	..	..	..	..	9	3	19	31
Total	..	..	..	..	94	52	54	200

There are a large number of "not known" cases in Group I, but even if these all had an I.Q. over 80, there would still not be a significant relationship.

PRESENT PERSONALITY

On entering an institution some 150 (75 per cent.) of these patients were considered to be emotionally disturbed. Of the 17 who are not now working, 6 with I.Q.s below 76 are not emotionally disturbed, leaving 11 whose disturbance is such that they cannot earn their own living. They are in fairly sheltered surroundings, in mental hospitals, or with relatives, and it is thought they would not be capable of living on their own and supporting themselves. Thus the emotional disturbance which was considered serious enough to stop them earning their own living seems to have declined from over 75 per cent. to less than 6 per cent. There are, however, a number living and working in the community who still find difficulty in relations with people and their work. Craft (1958) found similar figures in his survey of "Cornish defectives living in the community". He states that "of 100 surveyed, 6 patients were considered to be disabled by mental disorder" and "this finding supports the view that mental disorder is part cause of certification and admission to hospital among the dull".

DISCUSSION AND CONCLUSIONS

One of the main questions that must be asked is whether the original certification of these 200 women and their subsequent years in institutions have been beneficial or necessary, and, if not, how this could have been avoided. As the majority of patients came as adolescents and are now middle-aged, one is assessing and discussing the measures taken nearly twenty years ago of dealing with a problem that had fewer answers then than it has now. In many cases the use of the Mental Deficiency Acts appeared to be the only way of helping a girl. About three-quarters of the "feeble-minded" patients who came to this hospital were later discharged, so that it seems logical to re-orientate some institutions from long-term custodial care to short-term training homes or hostels. Since the majority of patients admitted lack parents and homes, the success of their rehabilitation will, to a great extent, depend on the ability of the social worker to provide substitutes for these. A considerable number might avoid going to institutions altogether if enough open hostels were provided for them.

The discharged women do not appear to be engaged in anti-social activities, nor are they a great burden on the community. There is an acute shortage of beds in mental deficiency hospitals at the moment and the pressure on the services can be greatly reduced by the discharge of women who are capable of managing their own lives. To predict those who are so capable is not easy and an element of chance remains. This can be substantially reduced by

maintaining good relations with the patients after they have left, so that they will return for help and advice if they are in difficulties, and by providing social workers to assist with these difficulties. At the Fountain Hospital one of the social workers deals with the after-care of all the adult patients in addition to other duties.

A similar conclusion to that made by Craft (1958) can be drawn from these patients—that for high-grade persons a diagnosis of mental defect applies principally to the young and has a good prognosis. It also seems likely that a very deprived “feeble-minded” adolescent can be expected to improve considerably in behaviour and personality as well as in intelligence quotient.

The discharge and the success rate at this hospital appears to be higher than that usually reported from other hospitals. This may be due to a number of reasons—firstly the intelligence of the women may have been higher than elsewhere and their emotional problems less severe; however, the majority originally came from other institutions and did not seem lacking in social problems. Secondly, the policy of allowing discharged patients to come back to the hostel on an informal basis may have helped. These informal admissions tend to work as a safety valve in the same way as any girl might stay at home between different jobs. One of the few features that are found universally among these discharged patients is the lack of a place to which they can return when things become difficult. Thirdly, competent social help was available promptly for all the discharged patients and this may well have made a considerable difference to the success rate.

There is some evidence that those patients with psychotic traits, although suitable for discharge, need more help than those who have transgressed the social code. This may merely reflect the fact that a more positive, aggressive type of personality needs less help than a timid, dependent type. However, it was in the past just these “bad-tempered”, “immoral” and “dishonest” patients who constantly rebelled against institutional life and were considered most undesirable and unsuitable for licence by the hospital authorities.

SUMMARY

The purpose of this survey was to assess the past history and intellectual ability of all the adult feeble-minded women discharged from this hospital and to make an interim report on the progress of their rehabilitation. It was found that the 200 women discharged by February, 1958 represented 70 per cent. of all admissions with an intelligence quotient over 50. The average age of certification for the discharged women was 22 and the average age at discharge was 35; they have now been living in the community for an average of 5 years. The average I.Q. of the 123 who were tested was 81 on the Wechsler-Bellevue Intelligence Scale. Only 11 per cent. of those tested had an I.Q. below 70. Their past history showed large numbers having physical handicaps, being illegitimate, losing their parents or having mentally disturbed parents. The cause of certification was investigated. It was found that 25 per cent. were certified mainly because of their illegitimate child. The lack of anyone to take responsibility for them in their late teens and early twenties was a very frequent factor. Seventy-five per cent. were stated on admission to have some kind of personality defect. Two patients have been re-certified; one of these went to another institution and has since been discharged and the other is working on daily licence. Contact has been maintained with 171 of the 200 women. About 20 have returned to the hospital for short periods. Roughly a third each

are living independently, are living in a resident post, or are living with relatives. Of those known, only 10 per cent. are not working or housewives, 46 are married; 70 of 200 have had 160 children. Since discharge, seven of the unmarried women have had children.

It is considered that roughly a third of the group need the social worker's help after the first few years.

The results seem to suggest that those who need least help are those described as immoral, beyond control, dishonest and bad-tempered; whilst those who need more help are those described as "inhibited", "hysterical", or those with psychotic features. Three-quarters were described as emotionally disturbed on admission; now there are less than 6 per cent. whose disturbance is such that they cannot earn their own living, although a number still find difficulty in their relations with people, and their work.

The material presented in this paper supports the view that the majority of those classed as "feeble-minded" in the past, and whose difficulties are in effect more social than intellectual, can be successfully re-established in the community.

ACKNOWLEDGMENTS

This is a description of the work of rehabilitation carried out by Dr. L. T. Hilliard, Miss M. Kerry, Mrs. L. Mundy and Dr. C. Williams with the help of the South Side Home nursing staff under Sister Trinder. I should like to thank them for their co-operation and advice in recording the results of their work. I should also like to thank Dr. B. H. Kirman, Dr. N. O'Connor, Dr. J. Stern and Dr. M. Woodward for reading and commenting on this paper and Miss N. Dickinson, Medical Records Officer, and her staff for their help.

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APPENDIX I

A composite picture of the typical case history which is built up as one reads through the case papers is given below:

A teenager is before the authorities. She has a father who is unstable, her mother died when she was about seven and she was looked after by another relative for a few years and then was in three or four different homes. As the time for her to leave school approached, it was realized that she was going to be a problem. She had no proper home or person who was responsible for her. She has temper tantrums and is always seeking affection. She has had a

number of changes of school and she is educationally backward with an appalling lack of arithmetical knowledge. She is short-sighted and has flat feet. The problem she presents is shelved for a few years by sending her to a training home, but she never settles there. She then begins to take an interest in boys, so it is decided that she must be certified as she will get "into trouble". The medical officer who certifies her considers that she is feeble-minded; he notices that she is unable to say how many halfpennies there are in 3s. 4½d. and does not know the name of three counties. She is not seen by a psychologist. When she is ultimately tested, it is found that she has an I.Q. of 84 and that she is an immature and unstable adolescent with a strong distrust of authority and no one she can turn to in place of her family. This girl spends 8 years in other institutions where she is not considered suitable for licence and then comes to the Fountain as a "working patient". This is, of course, an average picture with all the faults which come from telescoping information.

Reviews

The Clinical Examination of Patients with Organic Cerebral Disease. By ROBERT KLEIN and W. MAYER-GROSS. Cassell and Company Ltd., London, 1957. Pp. 96. Price 15s.

A sound knowledge of the disturbances of the higher cerebral functions is essential to the psychiatrist for the diagnosis, treatment and management of his patients. It is also of fundamental importance for the understanding of abnormal behaviour in general. Yet it is only too common for psychiatrists to misdiagnose aphasia as confusion or dementia. This important area of neuro-psychiatry is badly neglected today, even in the country of Hughlings Jackson and Henry Head. The authors of this excellent book deserve gratitude for presenting a guide to the study of disturbances of cerebral functions of the highest level of integration. Both authors speak with authority, having themselves made important original contributions in this field. It is of interest that Dr. Klein's first teacher was Alois Pick who pioneered the psychological approach in neuro-psychiatry. The book deals with the diagnosis and investigation of patients suffering from aphasia, agnosia, spatial disorientation, disorders of the time sense, apraxia, tactile agnosia and disturbances of the body image. It has a very useful bibliography. This book ought to be read and used by all students and practitioners of psychiatry, neurology, and geriatrics. Sir Russell Brain, in his appreciative foreword, rightly states that it fulfils a real need.

There is only one suggestion this reviewer would like to offer for the next edition, i.e. an alteration of the title which in its present wording does not clearly define the subject matter of the book.

E. STENGEL.

On the Mysterious Leap from the Mind to the Body. A Workshop Study of the Theory of Conversion. Edited by FELIX DEUTSCH. International University Press, New York, 1959. Pp. 273. \$5.

The book consists of contributions by fifteen workers one of whom was Stanley Cobb. The title was taken from Freud's Introductory Lectures. Felix Deutsch, the leader of the team, was the first physician who studied psychosomatic illness by the psychoanalytic method. In his opinion, the mental mechanism of conversion can cause physical disease and, on the other hand, physical disease can serve as an outlet for conversion symptoms. He and his co-workers do not distinguish between conversion symptoms without tissue change and psychosomatic illness in the accepted sense, such as gastric ulcer, ulcerative colitis, etc. They regard psychosomatic symptoms as symbolic representations of psychological processes. Symbolization can, in their opinion, alter physiological processes from an early age. Each part of the body possesses the potentiality for the symbolic expression of loss and separation of objects and their restitution. The application of this theory is illustrated by several case records. It is not shared by all psychoanalysts who have concerned themselves with this problem. Flanders Dunbar and Franz Alexander did not interpret psychosomatic illness solely in terms of highly structured psychological processes. Nevertheless, this book presents a bold, though not wholly convincing attempt at breaking through the psycho-physical barrier.

E. STENGEL.

Differential Treatment and Prognosis in Schizophrenia. By ROBERT D. WIRT, Ph.D., and WERNER SIMON, M.D. Charles C. Thomas, Springfield, Ill., 1959. Pp. 198.

This is a detailed report of a controlled therapeutic study of somewhat unusual design. An interim report was published in the *Amer. J. Psychiatry* (1958), 114, p. 1077.

Schizophrenic patients admitted to a Veterans Administration hospital for the first time were assigned to one of four treatment groups on a random basis, until each group consisted of 20 patients. The treatments were (1) chlorpromazine; (2) reserpine; (3) the most suitable according to clinical judgment, i.e. E.C.T., insulin coma or drug treatment; (4) hospital routine alone. The patients were evaluated psychometrically with a behaviour rating scale, the M.M.P.I. and the Shipley Hartford Scale. A social case-study was also undertaken, each case being rated on 12 prognostic factors. The result of treatment was assessed after 30 days and rated on a 9-point scale for improvement. After this evaluation the patients were given whatever treatment seemed indicated, unless they were fit for discharge. They were re-evaluated after a year. The authors found that the "clinical judgment group" did best. The second best was the chlorpromazine group. The reserpine group did worst. When the authors presented their interim report to the American Psychiatric Association they quite rightly came in for heavy criticism, mainly for the absurdly short evaluation period. The authors stated in reply that their design was statistically impeccable and that they would not have been justified in withholding indicated treatment from their patients for longer than 30 days.

E. STENGEL.

Group Psychoanalysis. By B. BODHAN WASSEL, M.D. Peter Owen, London, 1959. Pp. 306. Price 30s

The author, an American psychotherapist, has been guided mainly by the theory of Karen Horney who in the later part of her life had adopted a sociological and moral theory of the aetiology of the neurosis. She dissociated herself from what she called the "instinctivistic", i.e. fundamentally biological orientation of psychoanalysis. Neurotic trends, to her, were safety devices against potential dangers and most neurotic conflicts were culturally determined. Her theory had certain features in common with those of Adler, Jung, Sullivan, and the "anthropological" psychology of the existentialists. The strong emphasis on human relations made it readily applicable to group therapy. The neurotic, according to this theory, strives for superhuman perfection. Group therapy "helps him to recognize and conquer his illusions". It reveals "the unconscious neurotic pride and the illusion of omnipotence" which underlie the neurosis. It "analyses and resolves self-effacing and self-inflating neurotic patterns and gradually identifies, elicits and mobilizes the individual's healthy, holistic strivings". In the language of classical psychoanalysis, this school of psychotherapy is mainly concerned with the restoration of ego-functions, especially those highly valued by society. The strong re-educative orientation is likely to appeal to non-medical psychotherapists, of which there are many in the United States.

E. STENGEL.

A Mental Health Hand Book. By IAN SKOTTOWE. Edward Arnold, London, 1957. Pp. 196. Price 21s.

This book is intended for doctors, social workers, health visitors, mental health officers and others in public health departments whose work brings them into contact with the field of mental health. It ought to be obligatory reading for members of Management Committees of mental hospitals. It can also be recommended to medical students, general practitioners and to psychiatric nurses and their teachers. No other book covers the social and administrative aspects of psychiatry so fully and lucidly as this highly readable volume, which contains an amazing amount of information and wisdom. The following are the headings of the eight chapters: an introduction to mental health services; what is mental health? personality and constitution; natural experience and social cultures; the varieties of mental ill-health; some social repercussions and opportunities; towards prevention and treatment; organization, training, health education and research. The book was published before the passing of the new Mental Health Act which it foreshadowed. Far from making the book obsolete, the new Act has given it heightened topicality, because many of the problems so

lucidly discussed here have now become practical issues, and the number of people concerned with them is bound to grow rapidly as the result of the new legislation. The publishers will be well advised to enclose a note to this effect into the book, in case individuals or organizations should think that it is out of date.

E. STENGEL.

Schizophrenia. By MANFRED SAKEL. Peter Owen Ltd., London. Pp. 335. Price 35s.

The late Manfred Sakel was a tragic figure. His was a remarkable success story. An unknown young psychiatrist, he succeeded in persuading the all-powerful head of a famous psychiatric university institute to offer him all the facilities at his disposal for a new treatment of schizophrenia. Insulin coma treatment was soon adopted all over the world and opened up a new era in the treatment of the major psychoses. Sakel's place in the history of psychiatry is secure, whatever the fate of his therapy may be. Yet he was never satisfied with the kind of fame it brought him, and he died a deeply disappointed man. He wanted to be recognized not only as a bold pioneer in the field of therapy, but also as a scientist and thinker. Learned societies often appear ungrateful to the brilliant innovator who stimulates progress but refuses to submit to the discipline of science. This book explains why full scientific recognition was withheld from Sakel. It shows an amazing lack of humility and of other attributes of the scientific attitude. Much of the book makes embarrassing reading, especially the theoretical chapters in which the author propounds a peculiar brain mythology of his own. He firmly believed in the specificity of his treatment which "eliminates psychotic intercellular pathways". In his opinion, schizophrenia is caused by a dysfunction of "the insular and adreno-cortical system". The limitations of the treatment are not discussed. The "classical" method, which is described in detail, cannot have fulfilled his expectations, because later he recommended extremely prolonged comas in many cases. The value of this posthumous book, and of its companion volume dealing with epilepsy, is mainly historical. It tells a great deal about the man who shook psychiatry out of its therapeutic inertia.

E. STENGEL.

Family Worlds. A Psychological Approach to Family Life. By ROBERT D. HESS and GERALD HANDEL. University of Chicago Press, 1959. Pp. 306.

The authors, both of whom are social psychologists, have studied the problem how a family functions. There are the biologically determined universals of family life, and there are other features which are culturally determined. The latter show a greater variety than the former. Five "psycho-social family portraits" are presented in this book. The unit of study was the typical American "nuclear family", i.e. the parents with their biological children. The data were obtained by interviewing each member of the family. The TAT and a sentence-completion test were applied to each person. The authors found that each family had a "family theme", i.e. a pattern of feelings, motives and fantasies grouped about some concern, such as "flight from insecurity" or "demonstration of constructive independence", etc. They aim at a typology of family interaction patterns. This is a promising pilot study in an important area of research. Knowledge about the social aspects of normal family life is essential for the understanding of disturbed family relationships which so often become the concern of the psychiatrist.

E. STENGEL.

A Short History of Psychiatry. By ERWIN ACKERKNECHT. Translated from the German by SULAMMITH WOLFF. Hafner Publications Coy., New York and London, 1959. Pp. 98. Price 25s.

This is a useful little book which deserves to be widely read, especially by psychiatrists in training. The author, who is Professor of the History of Medicine in the University of Zurich, views psychiatry as a branch of medicine. He is also interested in its ethnological aspects. However, he tends to overrate the existing knowledge about

ethnological differences of mental disorders and he is unduly impressed by alleged fundamental changes in the character of mental illness in historical times. His observation that "the normal man of today would have seemed abnormal in many earlier centuries" comes oddly from a historian of psychiatry. The author does not say what he means by "the normal man of today". He has not made it sufficiently clear that in our time the scope of psychiatry has changed greatly. Psychiatry is no longer "the science of mental diseases", but has become the study of abnormal behaviour. Nor is there a reference to its relationship to psychology, which has been such an important feature of modern psychiatry, especially in the English-speaking countries.

These critical comments should not detract from the value of the book as a primer of psychiatric history. It contains a great deal of information and brings home to the reader that present-day psychiatry has much to be proud of. The translation is admirable.

E. STENGEL.

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Environmental Therapy of Chronic Schizophrenic Patients. <i>Ytrehus, A.</i> 126		
<i>Memory Disturbances After Electroconvulsive Therapy</i>		
Thirty patients were examined with one form of test battery a few days before the first, and with the other form one week after the last electroshock treatment in a series. The two forms of the test battery were used alternately before and after the treatments. The mean number of treatments was 3.6 over a mean period of 10.1 days. The test battery comprised the three memory tests for evaluation of reproduction immediately after learning and three hours later, described by Cronholm and Molander (1957), called the 30 word pair test, the 20 figure test, and the story test. Another, new test, using paired associates and intended to serve the same purpose, called the 15 letter-symbol pair test, was added to the battery. A vocabulary test was also given. After the series of treatments there was a significant decline in the measures on the operationally defined variable "delayed reproduction" (the number of items reproduced three hours after learning) in the word pair and the figure tests. In the word pair test there was also a significant decline in the score for "retention" (the quotient of the number of items reproduced after three hours over immediately) and a significant increase in the score for "forgetting" (the difference between the number of items reproduced immediately and after three hours). In the other tests no significant differences between the performances before and after treatment were found. It is concluded that the adverse effect on memory functions mainly affecting the hypothetical variable "retention", shown to exist six hours after the second treatment by Cronholm and Molander (1957), still persists one week after the termination of a series of treatments, but to a less degree.		
(Authors' Abstr.)		
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The Occurrence of Paranoid Incidents and Abstinence Delirium in Abusers of Amphetamine

During a period of ten years (1947-1957) 14 patients in all were admitted to Ullevål Hospital, Psychiatric Department for Men, for treatment for amphetamine addiction. Seven of these patients were hospitalized either with an acute paranoid psychosis or they had undergone one or more such psychoses prior to admission. This psychosis was of a temporary nature and disappeared in the course of a few days. None of the patients suffered from a lengthy schizophreniform condition. In the other 7, all of whom had abused other medication, no psychotic symptoms were apparent, but they showed other psychotic reactions (sleeplessness, irritability, suspicion) which were related directly to amphetamine.

In accordance with the pharmaco-dynamics of amphetamine, all the reactions may be understood as a continuum, where the individual disposition, the amount of amphetamine, and the admixture of other substances are the deciding factors for the nature of the reaction.

The psychotic reactions are regarded as special toxic psychoses, and it is suggested that they are connected with the effect of amphetamine on the mechanism of cerebral oxidation.

Four patients developed a delirium psychosis during the abstinence. It is shown that in these 4 patients a common symptomatology is evident, different from that seen in delirium occurring in alcohol addicts and abusers of barbiturates and opium. The characteristic difference is, in the first place, the lack of anxiety and the only slight pronounced vegetative symptoms, while activity and restlessness are greatly increased. There is also a lengthy period of latency and the delirium lasts longer.

It is concluded that it is probable that there is an abstinence delirium characteristic of amphetamine abuse, and that amphetamine is a drug which is as dangerous for addiction as other medication which can lead to toximania.

(Author's Abstr.)

Depressions in Patients Treated with Reserpine for Arterial Hypertension

After a review of the literature 11 female patients are mentioned, all hospitalized, who were suffering from depressions appearing after 1-10 months' treatment with reserpine in daily doses from 0.50 to 0.75 mg.; one patient had been given a whole-root preparation of Rauwolfia serpentina, containing 0.3 mg. reserpine. The patients were 42-76 years old (average 58.4 years). A predisposition for depressions is known in five patients. The symptoms were a deep sensation of unhappiness, frequent crying episodes, accompanied by restlessness and anxiety. In one case suicide was attempted. Seven patients had E.C.T., 2 patients a combination of E.C.T. and chlorpromazine, and 2 patients had only chlorpromazine. The treatment had good effect in all cases. Five-8 months after leaving hospital 2 patients had once more reserpine prescribed against arterial hypertension and were later readmitted to the hospital after relapse.

As the discontinuation of treatment with reserpine does not imply cessation of the symptoms, it is not supposed that reserpine can be the only cause of symptoms, but rather that it is a question of provoked endogenous depression.

(Author's Abstr.)

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Childhood Patterns Predictive of Adult Schizophrenia: A 30-Year Follow-up Study

A 30-year follow-up study of 526 children seen in a child guidance clinic shows that of the 284 so far interviewed, 10 per cent. were diagnosed in adult life as schizophrenic and

20 per cent. were diagnosed as no disease. The childhood histories and adult adjustment of the schizophrenic and no disease groups were compared. This comparison shows the following:

1. In childhood the schizophrenic group have more symptoms of all kinds than the no disease group including a large number of anti-social symptoms.
2. More areas of function were disturbed in the pre-schizophrenic child than in the child who in adult life had no psychiatric disease.
3. As adults the schizophrenics have a higher rate of mental hospitalizations than the no disease group.
4. The schizophrenic adults have a higher arrest rate than the no disease group. The schizophrenics are consequently often treated as criminals rather than mentally ill persons.

(Authors' Abstr.)

Iproniazid Chemotherapy in Melancholia

1. Chemotherapeutic remission of melancholia can now be accomplished, in a majority of cases, without resort to E.C.T., by carefully supervised administration of Marsilid (Roche), iproniazid (1-isonicotinyl, 2-isopropylhydrazine phosphate).
2. However, until methods are discovered for accelerating Marsilid's effectiveness in the first few days of treatment, the aggressively suicidal case must still be given E.C.T., which assures most immediate remission of depression. Each case must be carefully evaluated when first seen.
3. This chemical, introduced 6 years ago for the treatment of tuberculosis, is now found to possess much wider scope in medicine including therapeutic efficacy in some apathetic and withdrawn, seclusive types.
4. A major factor in effectiveness of this chemical in accomplishing psychic energization is the prevention of inactivation of the brain-stored powerful hormone serotonin, by its amine oxidase inhibitor action, but other equally powerful chemical interactions may be simultaneously involved.
5. The powerful chemical forces released may induce serious complications unless the physician psychiatrist is constantly alert to the need for frequent alteration of dosage as indicated by his physical findings.
6. Excellent antidotes for certain complications are available.
7. A by-product of major significance is the enhancement of psychotherapy through increased spontaneity, improved sense of well-being and resulting betterment of rapport.

A Hypothesis on the Possible Causation of Hepatitis in Association with Iproniazid

Without doubt the major enigma in administering Marsilid lies in the fact that in rare cases the iproniazid becomes bound in the brain in some unknown way. When this occurs even a small dose can push the B.P. very low and keep it there. The only antidote for this is cortisone, a fact that is not well known. It is these rare cases that may well have resulted in acute hepatitis and death since the B.P. may have remained low without the doctor's knowledge with hepatic anoxic effect inducing acute yellow atrophy.

In discussing this problem, a well-known pathologist, Dr. Edwin Albano (Coroner of Essex County, N.J.) pointed out that anoxia can cause acute hepatitis. Therefore, it is possible that anoxia alone may have been a mysterious X factor we have been seeking to explain through allergy or something else. Therefore it is quite possible that the liver damage cases that have been reported (with a few deaths) may have been due entirely to *anoxia*. How?

This study, although it contains a relatively small number of cases to be sure, establishes the incontrovertible fact that iproniazid has a *hypotensive* effect in the great majority of cases. The author's experience shows that this is so frequent that it is almost a universal effect.

There could be no possible way of determining continuously what the blood pressure level is over a 24-hour period for any patient, but it is perfectly possible that in the variable gyrations of the B.P. that could occur, any patient that shows marked gyrations as a result of this drug, irrespective of the dosage, could have hypotensive effect of such degree as to cause temporary anoxic effects in the liver. This might occur not only once but intermittently while the patient was taking the drug.

It is possible that in the rare fatal case, the outcome might have been prevented if B.P. determinations had been frequent, and excessive hypotensive effect thereby prevented by reductions in Marsilid dosage in accord with the degree of hypotension observed.

(Author's Abstr.)

Trilafon (Fentazin) in the Treatment of Chronically Psychotic Hospitalized Patients

1. Experience with a new "tranquillizer", Trilafon or perphenazine, in treating 90 chronically psychotic hospitalized female patients for a limited period is described.

2. The effects were noted during the period of active administration of the drug and then for a period after termination of the drug therapy. Seventy-two per cent. of the patients showed some degree of improvement; 15 per cent. rose above minimal clinical gains.

3. Side-effects were not serious, were controllable and no deterrent to therapy. The absence of jaundice, blood-dyscrasia and photo-sensitivity are noteworthy.

4. The overall impression is that Trilafon is a useful drug with possibly distinct advantages over the older "tranquillizers" in the treatment of chronically psychotic hospitalized patients. (Authors' Abstr.)

Atropine Coma: A Somatic Therapy in Psychiatry

A somatic therapy for the treatment of selected cases of mental illness is described. Coma is produced by the administration of massive doses of atropine and terminated by physostigmine. Increased accessibility, better contact with reality, and more appropriate affective responses are found immediately after termination of coma, persisting several hours, providing the opportunity for more effective psychotherapeutic assistance.

(Authors' Abstr.)

The Treatment of Depressive States with G 22355 (Imipramine Hydrochloride, Tofranil)

Over a three-year period, more than 500 psychiatric patients of various diagnostic categories were treated with imipramine hydrochloride. It was demonstrated that the compound has potent anti-depressant action. Best responses were obtained in cases of endogenous depression showing the typical symptoms of mental and motor retardation, fatigue, feeling of heaviness, hopelessness, guilt and despair. The condition is furthermore characterized by the aggravation of symptoms in the morning with a tendency to improvement during the day. Treatment with imipramine hydrochloride resulted in full or social recovery in a high percentage of the patients. As a rule, the initial response was evident within 2 to 3 days, while in some cases 1 to 4 weeks of therapy were required. In view of the symptomatic nature of the action of imipramine hydrochloride, therapy must be maintained as long as the illness lasts. The side-effects noted were relatively slight, and with the exception of one case of severe allergic exanthema necessitating discontinuance of treatment, no serious complications were encountered. In some cases of depression, particularly those associated with organic brain damage or schizophrenic psychosis, transitory states of agitation or exacerbation of the psychotic features were noted. These observations suggest the importance of a proper selection of the patients as to type and etiology of depression. While in a number of instances, neurotic, schizophrenic or other depressions were also benefited by the drug, particularly when used in combination with chlorpromazine, electroshock or psychotherapy, it is concluded that imipramine hydrochloride is primarily indicated and effective in the treatment of endogenous depression.

(Author's Abstr.)

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Effects of Nuclear Radiation

A news release from the World Medical Association contains information that because of the great concern of the doctors of the world over the problem of the possible ill effects of radiation from the testing of nuclear weapons, as well as "the hysteria which has developed chiefly from ignorance", the W.M.A. at the request of many of its 55 member medical associations set up a plan to keep the medical profession of the world informed of the facts.

To this end the W.M.A. secured the services of Dr. Lewis M. Orr, of Orlando, Fla., consultant to the Institute of Nuclear Studies, Oak Ridge, Tenn., to address the 12th General Assembly of the W.M.A.

Dr. Orr reminded his audience that processes involving radiation were necessary in the diagnosis and treatment of disease and that "some hazards are implicit in almost all technological advances", and that the use of the X-ray for example in diagnosis, treatment and research is "for the benefit of mankind and can be controlled". It must not be discontinued.

Turning to the hazards of radiation fallout, and in particular to the genetic effects of strontium 90 as compared to the amount of radiation to which the human race has been subjected from natural sources, as well as from tests, the report is mathematically more specific: "the 30-year dose to the gonads received by the average person in the United States of America is estimated to be (a) from background radiation—about 4.3 roentgens, (b) from X-ray and fluoroscopy—about 3 roentgens, (c) from nuclear weapons testing if continued at the rate of the last five years—would give a probable dose of only 0.1 of one roentgen. If nuclear testing were continued at the rate of the two most active years the possible exposure of 30 years would be only about 0.2 of one roentgen."

Dr. Orr gave the opinion that every possible precaution should be taken in making nuclear tests, but that properly controlled testing that could contribute to knowledge and be beneficial to all people in many fields of investigation should not be discontinued.

It is gratifying to note that the report issued by the W.M.A. is in substantial agreement with that of an investigation carried out by the United Nations Scientific Committee.

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The Communication of Suicidal Intent: A Study of 134 Consecutive Cases of Successful (Completed) Suicide

1. A study of the communication of suicidal ideas by 134 consecutive suicides has been done by means of systematic interviews with family, in-laws, friends, job associates, physicians, ministers, and others a short time after the suicide.

2. Two striking findings were that over two-thirds (69 per cent.) of the suicides had communicated suicidal ideas and that 41 per cent. had specifically stated they intended to commit suicide. In the majority of instances, the suicidal communications were of recent onset (months), repeatedly verbalized, and expressed to many persons.

3. Another striking finding was that 98 per cent. of these persons were probably clinically ill prior to their suicides.

4. The frequency of expression of suicidal ideas was not significantly related to age, sex, marital state, religion, whether living alone or not, clinical diagnosis, occupational status, income, or education. Chronic alcoholics had a somewhat greater tendency than the other diagnostic groups to make the specific statement that they intended to commit suicide.

5. The communication of suicidal ideas was analyzed as a general system of communication with reference to experimental psychological studies.

(Authors' Abstr.)

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Releasable Histamine Levels and Histamine Tolerance in Tissues of 291 Psychotic Patients

1. Skin histamine, releasable on intradermal injection of curare, and tolerance to intradermally injected histamine have been studied in 291 mental patients and 51 normal subjects.

2. The data were analyzed statistically for the effect of sex, age, duration of hospitalization, drug treatments and diagnosis. Data from patients were also compared with normal subjects.

3. Releasable skin histamine was the same in male and female patients but tolerance to histamine was greater in males.

4. Age did not affect releasable skin histamine levels except in the 50-59 year old group as compared with the over 60 group. The difference was not striking but indicated a trend toward less skin histamine in the older age group. Tolerance to injected histamine was not affected by age.

5. Duration of hospitalization, which may be a rough approximation of duration of mental illness, did not alter skin histamine content or tolerance to histamine.

6. Reserpine lowered skin histamine very considerably and was unique among the tranquilizing drugs in this property. Both reserpine and chlorpromazine increased the tolerance to histamine.

7. Schizophrenics and manic-depressives did not differ in skin histamine levels or response to intradermally injected histamine.

8. Patients receiving reserpine therapy had a lower level of skin histamine than normal but patients not receiving drugs and patients receiving drugs other than reserpine did not differ from normals in releasable skin histamine. Histamine tolerance was greater in patients receiving drugs in general, or reserpine in particular, than normal individuals. Normal individuals and patients not receiving drug therapy gave similar responses to intradermally injected histamine.

9. An hypothesis is suggested for reconciling the infrequency of allergic reactions in psychotics with essentially normal releasable skin histamine and normal tolerance to intradermally injected histamine.

(Authors' Abstr.)

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The Symptomatic Relief of Anxiety with Meprobamate, Phenobarbital and Placebo

Fifty-two psychoneurotic out-patients with anxiety symptoms were treated in a controlled clinical study with meprobamate 400 mg. q.i.d., phenobarbital 16 mg. q.i.d. and placebo q.i.d. The patients were divided into 2 comparable groups of 26, each group treated by a different psychiatrist.

In the combined population of 52 patients, no significant differences appeared in the effectiveness of the 3 agents. The data then were analyzed for each psychiatrist's group

separately. In one psychiatrist's group, the 3 agents were equally effective. In the other psychiatrist's group, the 2 active drugs were equally effective, but superior to placebo.

Differences in the expectations of the two psychiatrists are discussed as a possible factor in these results, despite successful operation of the "double-blind" technique.

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Marsilid (Iproniazid) and Electroshock

Marsilid (iproniazid), so far, is the only drug with powerful anti-depressive properties. Twenty-five out of 32 patients derived benefit from the drug. It is helpful in depressive syndromes in which somatization and retardation predominate, particularly so, if strong neurotic features are present. In one severe chronic schizophrenic syndrome Marsilid had a powerful euphorizing, unblocking effect. It is ineffective in most agitated depressions. It requires considerable length of time before exerting effect. Half of the successfully treated patients relapsed and had to be kept on maintenance therapy.

Toxic features are of considerable degree and frequency. Fifteen out of 32 patients showed serious complications, among them 7 cases of liver damage. The well-known minor complications occurred in the vast majority of patients.

Indications for electroshock and Marsilid will rarely overlap since depressions with neurotic features were never a first choice indication for electroshock, and since the prevalent group of psychotic depressions, the agitated depressions, failed to respond to Marsilid. It appears that the anti-depressive effect of Marsilid is exerted over the sense of increased physical well-being and increased energy induced by the drug. A possibly important chance observation was the disappearance of the manifestations of psoriasis of 40 years uninterrupted duration and their reappearance after discontinuation of the drug.

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Studies in Multiple Sclerosis. I

The investigations presented here show that a study of the blood and cerebrospinal fluid from patients with multiple sclerosis presents a clear change in the distribution of the globulins in the cerebrospinal fluid, in the lipid content of the cerebrospinal fluid in the direction of an increase in cholesterol, and an abnormal distribution of lipoproteins in the cerebrospinal fluid without corresponding change in the blood.

A reduced cholinesterase activity in the cerebrospinal fluid was found, as well as a rise in the neuraminic acid content of the cerebrospinal fluid followed by a reduced amount in the blood. There was also a slight increase in the iron content of the cerebrospinal fluid in a few individuals, as well as an abnormal distribution of copper and neuraminic acid with respect to the proteins.

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Cortical and Subcortical Electrical Effects of Psychopharmacologic and Tremor-Producing Compounds

1. The administration of chlorpromazine was invariably followed by the appearance of slow activity of increasing voltage which was very similar to that of natural sleep. This change was not seen following reserpine.
 2. Of the subcortical structures studied, the intralaminar nuclei of the thalamus showed the greatest response to chlorpromazine and the hippocampus the least. The globus pallidus showed less slowing under chlorpromazine than during natural sleep.
 3. Within the limits of testing, chlorpromazine had little effect on the electrical response to sensory stimulation.
 4. Seizure-like activity sometimes followed the administration of either chlorpromazine or reserpine, but was more frequently seen after the latter.
 5. The cortical and subcortical electrical effects of four compounds (chlorpromazine, reserpine, Tremorine and pentobarbital (Nembutal)), each capable of producing tremor under various conditions, showed very little resemblance to one another.
 6. Potentiation of cortical fast activity normally produced by Tremorine, when pentobarbital was added to the same preparation, correlated to a fairly high degree with the persistence and amplitude of the tremor was seen clinically. Conversely, the "competitive" effects of chlorpromazine and Tremorine in combination frequently were manifested by subsidence of the tremor.
 7. Present results do not allow the conclusion that activation of the midbrain reticular formation may be evoked as the mechanisms of chlorpromazine or reserpine tremor.
- (Authors' Abstr.)

Evoked Electrical Activity of the Brain During Hypothermia

The retina, optic tract, lateral geniculate body, and visual cortex of the cat were stimulated optically during hypothermia. A progressive decrease in the responsiveness of the visual system was observed. This was manifested as an increase in the latency and as a decrease in the amplitude of response. These changes were reversible with re-warming. The average rate of change in the retina was greater than the average rates of change observed in the optic tract, lateral geniculate body, and visual cortex. A high degree of correlation was shown to exist between the latency and the amplitude of response in the visual system during the cooling-rewarming cycle.

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Pallidotomy and Pallidoamygdalotomy in Certain Types of Convulsive Disorders

Pallidal lesions or combined lesions of pallidum and amygdala were produced in stages in nine epileptic patients selected because anticonvulsive medication was ineffective, and seizure discharges were demonstrable in the basal ganglia by means of depth electroencephalography.

The study of simultaneous electrograms from the scalp and from the basal ganglia showed variable time relationships; in some instances there were apparently simultaneous discharges in all these areas; in others, the scalp discharges preceded; in a third type, they followed the basal-ganglia discharges. This third type suggests the existence of subcortical foci producing secondary cortical discharges.

The post-operative observation period was four months to over two years. Unilateral pallidotomy was sufficient in two of four cases to control the seizures or to diminish their frequency. In one instance bilateral pallidotomy stopped generalized tonic-clonic seizures and drastically reduced the minor attacks. After unilateral pallidoamygdalotomy, in three cases the frequency of the seizures was significantly diminished; in a fourth, this procedure combined with a small lesion in the anterior part of the opposite pallidum was insufficient. For a proper evaluation of the possible therapeutic value of these procedures long-range observations will, of course, be necessary.

The favourable effect of pallidotomy was particularly striking in the so-called salaam convulsions of children. This observation seems to suggest that the basal ganglia play an important part in the mechanism of this poorly understood type of seizures.

The favourable effects of pallidotomy and pallidoamygdalotomy may be due to interruption of corticofugal impulses in the basal ganglia and/or to elimination of subcortical epileptogenic foci.

(Authors' Abstr.)

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Dystonia Musculorum Deformans Alleviated by Chemopallidectomy and Chemopallidothalamectomy

Dystonia musculorum deformans, which has previously been demonstrated to be a progressive incapacitating disease of childhood, characterized by involuntary movements and deformities of the entire body, has heretofore been considered to be unresponsive to medical, surgical, physical, or psychiatric therapy. This investigation demonstrates that dystonia musculorum deformans in children can be alleviated by sufficient-sized, accurately placed lesions in the globus pallidus and/or ventrolateral nucleus of the thalamus.

During the course of this investigation, 16 children with advanced dystonia musculorum deformans were subjected to chemopallidectomy and/or chemothalamectomy. In three cases operation was carried out bilaterally. Thirteen of these sixteen cases demonstrated marked alleviation and reversal of the involuntary movements and deformities of this disease. Documented case reports illustrating this alleviation are included in this report. Such relief has now persisted for more than two years in several of these cases. The disease entity of dystonia musculorum deformans can no longer be considered as a hopeless, irreversible disease. The treatment of choice of dystonia musculorum deformans is chemopallidectomy and/or chemothalamectomy.

(Author's Abstr.)

Studies on Lysergic Acid Diethylamide

Pre-treatment with the neurohumoral blocking drugs phenoxybenzamine (Dibenzylamine), scopolamine, and 1-benzyl-2-methyl-5-methoxytryptamine (BAS) did not attenuate or accentuate the lysergic acid diethylamide (LSD-25) psychosis in man.

(Authors' Abstr.)

Effect of Some Indolealkylamines on Man

Snuff prepared from seeds of *Piptadenia peregrina*, of Puerto Rico, has not been found capable of producing the intoxication attributed to it by natives or by explorers, who have described the use of these seeds under the names cohoba, parica, yopo, and niopo. Two major constituents, bufotenine and dimethyltryptamine, did not appear capable of inducing the reputed action of the snuff, or that of *Amanita muscaria*. Bufotenine, up to 20 mg. intravenously, did not produce hallucinations in schizophrenic subjects, despite profound EEG changes, loss of consciousness, and intense peripheral action of serotonin character. Dimethyltryptamine had less intense physiological action but, above 20 mg. given intravenously or intramuscularly, eruption of preconscious ideations occurred. The action of both compounds was very rapid in onset and of brief duration. The compound 3-(3-dimethylaminopropyl) indole had no physical or psychological effect when given up to 70 mg. intramuscularly.

(Authors' Abstr.)

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Acetylcholine in the Mechanism of Headaches of Migraine Type

By use of a sensitive and specific bioassay method, an acetylcholine-like substance was detected in the cerebrospinal fluid of five of nine patients during headache of the migraine type presumed to arise from dilatation of intracranial arteries.

No such substance was found in specimens from a group of 28 patients with extracranial vascular headache or headache due to nonvascular or uncertain mechanisms; none was detected in specimens from patients with miscellaneous other neurologic disorders, except for two patients with epileptic illnesses, confirming earlier reports.

The results are consistent with, but do not prove, the hypothesis that acetylcholine or a closely allied substance is an active participant in the mechanism of headaches of the migraine type.

(Author's Abstr.)

Studies With a New Hallucinogen

Dosage-response data for some effects of N-ethyl-3-piperidyl benzilate (JB 318) are described.

With doses in the range of 5 to 15 mg. given orally in humans, atropine-like peripheral autonomic effects were induced.

Following administration of the same doses, anxiety, somnolence, illusions, visual and auditory hallucinations, decreased immediate recall, and feelings of "unreality" or a "dream-like" state predictably occurred.

Tactile and olfactory hallucinations, delusions, and ideas of reference were at times noted, but were not predictable in their occurrence.

In doses of 20 mg. or greater, it is likely that a true toxic delirium is induced by this agent.

The peripheral autonomic effects and psychotomimetic effects paralleled each other in intensity.

Individual differences occurred in degree and type of hallucinations and illusions.

Experiences of the immediate past or of early childhood largely determined the subject matter of the illusions and hallucinations.

(Authors' Abstr.)

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Study of Excretion of 5-Hydroxyindoleacetic Acid in Mental Patients

Reserpine, 2 mg. twice daily, was administered to 11 schizophrenic patients and to 6 high-grade mentally defective patients. The excretion of 5-HIAA was increased on the first day of medication in both groups of patients.

The excretion of the serotonin metabolite after the first day of medication and after its cessation was reduced to premedication levels or less.

When these patients were given a second or third course of reserpine at a later date, the excretory pattern of 5-HIAA was essentially the same as during the first course.

The most consistent feature of the experiments was the marked rise in the excretion of the serotonin metabolite on the first day of reserpine medication.

(Author's Abstr.)

Studies of Sleep Deprivation—Relationship to Schizophrenia

The clinical observation that a few schizophrenic episodes are preceded by prolonged insomnia led the authors to postulate that sleep deprivation, although a consequence of the emotional turmoil, might play a critical role in the precipitation of some psychoses. Therefore, studies were made of normal subjects who were kept awake for 72 hours. The setting was a social one, where anxiety was kept minimal. Changes on psychological tests were insignificant, but behavioral and subjective alterations were considerable. Feelings of depersonalization, illusions, hallucinations, disturbances in time perception, and auditory changes were common. Despite the long period of wakefulness, adrenocortical activity remained normal.

In another study subjects were kept awake for 48 hours and then given small amounts of LSD-25. Sleep deprivation markedly enhanced the ego-disruptive effects of the drug. It is suggested that sleep deprivation, when combined with isolation and incapacitating anxiety, may have a pathogenic potential that has not been adequately appreciated.

(Authors' Abstr.)

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Cerebral Atrophy Associated with Boxing

While neuropsychiatric complications in boxers are well known and subject to increasing interest, the cerebral pathology has not been fully explored, particularly with regard to the late sequelae.

Two patients with the symptoms of dementia pugilistica were studied.

Cerebral cortical biopsy in one case revealed mild neuronal degeneration and definite plasmatic gliosis in the lower cortex.

The brain of the other patient was severely atrophic, presenting a picture which grossly and microscopically resembled Pick's disease.

As in other cases, the disease became manifest some years after cessation of professional boxing.

In the absence of focal lesions, the pathogenesis is explained best on the basis of a thixotropic process, leading to premature aging of the brain.

These cases emphasize the complexity of the pathologic processes and the desirability of careful examination of the brains of former boxers.

(Authors' Abstr.)

Studies of the Hypoglycemic Brain

1. Severe insulin hypoglycemia does not lead to any appreciable change in the total deoxyribonucleic acid or the pentonucleic acid content of the brain.

2. The "protein-side-group ionization" of cerebral protein is unaltered.

3. The pattern of the cerebral free amino acids is altered in hypoglycemia. Glutamic acid is markedly decreased; γ -amino-butyric and alanine are also reduced, but to a less extent. Aspartic acid increases during the early stages but later decreases. Aminoacetic acid (glycine) is slightly increased.

4. There is a small tendency for the total nitrogen and acid-soluble nitrogen of the brain to decrease during hypoglycemia.

5. The energy that might be made available from the changes in the cerebral protein, free amino acids, and nucleic acids could supply only a negligible fraction of the total cerebral energy requirement of the brain in the hypoglycemic cat.

(Authors' Abstr.)

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Penicillin Treatment of General Paresis (Dementia Paralytica)

1. Repository penicillin is quite as suitable as aqueous penicillin for the treatment of general paresis (dementia paralytica). Although the minimal effective dose is unknown, the present study permits the pragmatically important conclusion that 6,000,000 units is ample.

2. Penicillin prevents paresis. None of the present group of 1,086 patients had received penicillin for early syphilis. Paresis has not been observed to develop after the penicillin treatment of asymptomatic neurosyphilis.

3. The present study cannot be said to reflect the effect of penicillin alone; rather, it presents only the effect of penicillin with or without fever therapy on a mixed group of paretics, a small, but undetermined, number of whom already had a process apparently arrested by other types of therapy before penicillin was given. That this detracts from the accuracy of the absolute percentages cited cannot be denied, but that it significantly affects the order of magnitude seems unlikely.

4. The trend in recent years in the United States has been toward the treatment of general paresis with penicillin alone. The possible additive effects of fever therapy are not sufficient to justify its use in any significant number of patients. The early diagnosis and prompt penicillin treatment of incipient paresis will result in clinical remission and ability to work in

more than 80 per cent. of patients, and will prevent practically all deaths from neurosyphilis. Even the severely affected or institutionalized patient has 1 chance out of 3 for improvement and rehabilitation for work. In contrast to the dire prognosis of untreated paresis, only 9 per cent. of penicillin-treated paretics are dead of neurosyphilis 10 years after treatment. Even so, the penicillin-treated paretic has nearly four times the death rate of his or her nonsyphilitic age, race, and sex counterpart.

5. The effects of treatment upon the individual symptoms and signs of paresis are, in general, strikingly beneficial. In the majority of cases, however, impairments of speech, insight, calculation, judgment, and general information do not entirely disappear.

6. Paresis strikes most frequently during life's most productive years. It is seen approximately three times as frequently in men as in women, and over twice as frequently in white persons as in Negroes. The usual incubation period is 10 to 24 years after infection, with a spread from 2 to more than 30 years. The simple demented type of psychosis is more frequent than all other types combined. In the absence of previous treatment the spinal fluid Wassermann reaction is always positive, usually with small amounts of fluid, and the spinal fluid cell count is almost always elevated. The blood serologic test may rarely be negative.

7. In general, more than one adequate course of penicillin (6,000,000 units or more) is of no demonstrable additional value in the treatment of paresis. Absence of clinical improvement, persistently abnormal spinal fluid protein level, or persistently positive spinal fluid Wassermann reaction are not indications for re-treatment. Re-treatment with penicillin is indicated under the following circumstances: an initial course of therapy of less than 6,000,000 units, temporary clinical improvement following an initial course with subsequent clinical progression, or spinal fluid cell count of 5 or more after the first post-treatment year. The essentially identical probabilities of death in patients who received one course of treatment and in patients who received more than one is strong evidence against the value of routinely repeated courses of penicillin in the treatment of paresis.

8. Herxheimer reactions, notably exacerbation of the paretic psychosis or convulsive seizures, occur more frequently in the presence than in the absence of spinal fluid pleocytosis. Pre-treatment sedation and often the use of anticonvulsants are advisable. The Herxheimer reaction does not cause long-term damage in paresis.

9. The diagnosis of paresis will frequently be missed if formal pre-treatment examination of mental status is omitted. Indeed, it may be stated that skilled neuropsychiatric examination affords definite prognostic data as to the probability of improvement in psychosis, rehabilitation for work, and, to a certain extent, death itself.

10. Progression and death due to neurosyphilis occur almost altogether in patients with severe pre-treatment psychoses. Post-treatment psychiatric hospitalization is directly proportional to, and clinical improvement and rehabilitation for work are inversely proportional to, the severity of pre-treatment psychosis. Type of psychosis is of less importance prognostically than is severity of psychosis. The shorter the duration of paretic psychosis at time of treatment, the more frequent is clinical improvement and rehabilitation for work.

11. The presence at times of treatment of incontinence, inability to dress self and perform other simple acts of personal toilet, and, to a less extent, of convulsions, affords a particularly poor prognosis for longevity.

12. Work status at time of treatment is of great prognostic import. Of perhaps equal significance is the length of time which has elapsed since the patient has been able to work at his usual occupation.

13. Age within the limits of 30-59 years, race, and sex are relatively unimportant factors in the prognosis of paresis.

14. Pre-treatment pleocytosis indicates an active inflammatory process more susceptible of improvement by treatment, but in a minority of cases leaving behind sufficient brain damage to nullify any real clinical effect. The absence of pleocytosis indicates a relatively static process less susceptible of improvement but, at the same time, less likely to progress. Pre-treatment spinal fluid protein levels are of less prognostic import.

Persistent cell counts of 11 or more were not usually encountered after penicillin treatment. Clinical progression did, however, occur significantly more frequently with persistent cell counts of 5 to 10 than with cell counts of 4 or less. Persistent spinal fluid protein elevations were relatively frequent, but of no prognostic import.

(Authors' Abstr.)

The Pathology of Schizophrenia

The conclusion seems inescapable that no specific change in any tissue or system of the body has been demonstrated that can account for the clinical syndrome of schizophrenia. Even nonspecific histological changes appear to be rarely found, and, when detected, to be unrelated to the psychological derangement. The vast body of literature on the subject falls into two categories: positive pronouncements of anatomical alterations believed to be responsible for the pathogenesis of schizophrenia, and negative reports demolishing this claim. As noted in each of the four successive periods of this review, the great majority of well-controlled and critical studies fall in the latter category. As far as was possible, the reports selected to represent the two categories in any of the four periods have been allowed to speak

for themselves, often in the original author's words; this apposition of one type of work or of one sort of conclusion against another has usually made criticism self-evident, and has absolved the reviewer from the necessity of commenting on each paper separately.

At the end of the longest, most recent review of the subject, the author (Peters) lamented: "The result of this communication is unsatisfactory. The basic pathology in schizophrenia, as in idiopathic epilepsy is not clear." It is pertinent that Peters does not restrict his remark to histopathology; in the term "basic pathology" he probably includes physiological pathology and metabolism as well, implying that the pathogenesis of schizophrenia is not clear. Whether agreeing or disagreeing with this generalization, and without attempting to review all aspects of the currently popular and already extensive subject of biochemistry and metabolism in schizophrenia, the research worker of today might profitably take stock of his specific field of interest and make sure that thought and theories are not passing for facts and things.

At the risk of sounding pessimistic, it appears to the author that it is the lesson of the past that history repeats itself. One need not be shocked, therefore, if the current notion of there being a distorted molecule behind a distorted thought is as difficult to demonstrate as the older belief of a defective neuron behind a defective thought.

(Author's Abstr.)

Effects of Imipramine (Tofranil) on Depressive States

Imipramine, an iminodibenzyl derivative, was given to 145 patients, consisting of 126 with depressive states and 19 with other mental syndromes, with an average oral daily dose of 100 mg. and an average duration of three months.

The depressive states consisted of 98 "typical" and 28 atypical cases. In the former group 82.6 per cent. showed marked to moderate improvement and in the latter group 67.0 per cent.

There was a therapeutic lag of three days to three weeks before the clinical response would become manifest. The optimum period of therapeutic trial was about three months. Side-effects were minimal.

The specific changes concomitant with imipramine administration were investigated in 10 closely observed patients. These were the disappearance of feelings of guilt; a change from feelings of helplessness to those of hopefulness; a change from relatively excessive pre-occupation with internal object relations to a relatively optimal pre-occupation with external object relations; appearance of elation in eight patients, hypomanic state in one patient, and manic state in another; an increased ability to express aggression; the disappearance of the need for alcohol intake in four alcoholics; the lack of alteration in basic, predepression personality structure, which reappeared after the relief of depression. Based upon these observations, a dynamic hypothesis was forwarded that concomitantly with imipramine administration a change in the direction of aggressive drives and aggressive cathecting energies seemed to occur in relation to the internal object system of control (superego elements).

(Authors' Abstr.)

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Corticobulbar Connexions to the Pons and Lower Brain-stem in Man. An Anatomical Study

The distribution of degenerating fibres was studied in the medulla oblongata and the pons of four human brains, in which either an encephalomalacia was present, due to occlusion of the middle cerebral artery, or a haemorrhage in the internal capsule. This was done with the aid of the Nauta-Gygax silver impregnation technique.

In these brain-stems, many degenerating fibres were distributed to the trigeminal motor, facial, hypoglossal and supraspinal nuclei, whereas the spinal accessory nuclei received only

a few degenerating fibres and none were present in the abducens nuclei. In view of its clinical importance, the distribution of degenerating elements throughout the ipsilateral facial nucleus was studied in more detail.

Moreover, the accumulation of degenerating fibres and end-ramifications present in the dorsal grey substance of the spinal cord, was found to continue rostralwards throughout the entire lower brain-stem. Degenerating elements were observed in the region ventral to and in the "hilus" of the nuclei cuneatus and gracilis, as well as in the spinal trigeminal complex and the lateral tegmentum up to the level of the isthmus. In addition, degenerating fibres were found to be distributed to the ipsilateral pontine tegmentum, the medial part of the tegmentum of the medulla oblongata as well as to the lateral reticular nucleus of the medulla, predominantly contralateral to the lesion.

A similar distribution of degenerating elements was found earlier (Kuypers, 1956, 1958) in the cat, after either lesions of the motor cortex or hemispherectomy. However, in this animal, the degenerating fibres to the motor nuclei were almost completely lacking. In view of these and more recent findings in the monkey, it would appear that specifically the fibres to the lateral tegmentum represent the corticofugal link in a phylogenetically older indirect corticonuclear pathway interrupted by one or more synapses in this region, and which in man is paralleled by a more recent direct corticonuclear system.

(Author's Abstr.)

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Neuropathic Observations in Phenylketonuria

Neuropathologic examination of the brain of an 18-year-old patient with phenylketonuria reveals multiple areas of altered myelination associated with variable degrees of fibrillary gliosis. The pertinent literature has been reviewed, and on the basis of this as well as previously published case reports it is concluded that the underlying pathogenetic defect in phenylketonuria may be a metabolically determined disturbance of the glial cell-myelin sheath relationship.

Neuropathologic observations indicate that this disease should be classified with the leucodystrophies and the cerebral lipidoses in the general group of dysmyelinating diseases.

(Authors' Abstr.)

Sudden Bodily Jerks on Falling Asleep

Many normal people occasionally, when falling asleep, experience a sudden jerk of the whole or a part of the body, sometimes accompanied by a vivid sensory experience.

Recordings of electroencephalogram, electrocardiogram, respiration and limb movements have been made during a number of these jerks. The jerks have only occurred during light sleep, often of very brief duration. They have sometimes appeared as part of an arousal response to a faint but significant external stimulus. They sometimes have occurred during

apparent small K-complexes in the EEG. A sudden, sharp, expiratory movement has sometimes immediately followed the jerk; alternatively a more delayed deep inspiration.

The jerks seem to occur, with widely varying frequencies, in nearly every normal person. The view that, when frequent, they should be classed as epilepsy, is critically considered.

(Author's Abstr.)

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Inequality of Palpebral Fissures Before and After Onset in Multiple Sclerosis (A Preliminary Report)

A gross inequality of palpebral fissures was observed in approximately 92 per cent. of 51 patients with multiple sclerosis. The inequality was usually due to ptosis, most often combined with a homolaterally small pupil. The high incidence of this inequality in multiple sclerosis has escaped previous observation, although true Horner's syndrome is generally known as an occasional occurrence.

The question arose whether this finding was or was not a consequence of the disease. Patients were therefore asked for full-face photographs taken prior to the onset of the disease, starting as early in life as possible. Satisfactory prior photographs were studied in 65 cases. Marked inequality was found in approximately 80 per cent. of the group. Usually it was due to ptosis. Pupils could rarely be carefully observed in these pictures.

Study of the photographs was made as follows: enlarged copies (not too much enlarged to obscure clarity of detail) were made of the ocular portions of photographs. These enlargements were studied in two ways: (1) for gross differences in palpebral fissures and for gross evidence of ptosis and of lower lid elevation; where possible, pupils were observed. (2) Careful drawings of lid-edges and irides were made by projecting the enlargements from an epidiascope; these drawings were then used for measurement of maximum interpalpebral differences.

A control study was made from approximately 360 photographs in college and other yearbooks. These photographs were comparable in quality to those of the patients. The control study was deemed necessary because of the commonness of fissure inequality in the general population. Definite inequality of a magnitude comparable to that characteristic of the multiple sclerosis series, was limited to slightly less than 30 per cent. of the controls. Minute narrowing was also more abundant in the multiple sclerosis than the control series. The difference between controls and patients was not only striking, but had a high degree of statistical significance.

The narrowing of the fissure in pre-onset pictures of patients, often may be seen as far back as infancy.

(Author's Abstr.)

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Evaluation of Therapeutic Results of Electric Stimulation of the Diencephalon

The aim of this study was to evaluate selective electric stimulation of different brain areas. Choice of cortical or diencephalic areas had been made possible by the use of special electrodes (naso-pharyngeal electrodes) which can be brought close to the centre of the base of the skull. This method (diencephalic stimulation) with currents of varying intensities, has been practised on several hundred cases of various diagnostic categories and the results tabulated.

It was found that the effects of diencephalic stimulation differ in a characteristic and repeatable manner from the effects of E.C.T. (cortical stimulation).

It was noted that in cases where anxiety and excitement were predominant symptoms, the diencephalic approach produced better results. Neurotic anxiety states as well as manic psychoses usually respond in one to five treatments with minimal currents (one to 3 ma.) with the Reiter machine.

Paranoid conditions with delusions and hallucinations seemed to respond better to a longer series (8 to 15 treatments) with higher currents (up to 15 milliamperes). The diencephalic approach never produced confusion nor memory loss and the EEG remained normal.

Depressive states clear up better with conventional electrode placement on the outside of the skull and higher currents (cortical approach).

Some schizophrenic reactions, particularly chronic conditions previously unimproved, have shown remarkable improvement or complete remission with a combination of cortical and diencephalic approach.

A tabulation of treatment results on 280 patients in Arizona State Hospital was given.

It is concluded that therapeutic results of conventional E.C.T. can be improved by the selection of treatment techniques which vary in local electrode placement, as well as in intensity and quality of current used.

(Author's Abstr.)

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The Mode of Action of Taraxein and LSD

Cerletti summing up the pharmacodynamic properties of LSD suggests that the psychotomimetic part of the LSD effect might involve a "trigger function". Heath, *et al.*, after a series of experiments in monkeys with taraxein followed by Kabi 888 and adrenolutin according to the authors' technique discuss various possibilities of the mode of action of taraxein, e.g. interference with amine metabolism or permeability changes of the blood-brain-barrier. Our experiments discussed above suggest that taraxein and LSD both have the property of enabling certain intravenously injected drugs to act on selected brain centres, not normally accessible to them. Endogenous compounds present in the blood might also produce behavioural changes through the same mechanism.

(Authors' Abstr.)

The Use of Glucagon in Terminating Insulin Coma

The absence of untoward reactions indicated a high degree of safety. Glucagon produces a slow, gradual, and smooth termination of coma in contrast to the sudden awakening with intravenous glucose. No prolonged coma occurred. Tube feeding was not necessary. The outstanding advantage of Glucagon over intravenous glucose was the increased ease of injection, 5 c.c. intramuscularly vs. 50 c.c. of 33 per cent. glucose given intravenously. With Glucagon there was no local reaction when given intravenously or better still, intramuscularly.

(Authors' Abstr.)

A Clinical Study of Marsilid in Psychotic Depressed Patients

The administration of iproniazid to eleven female psychotic patients with depressive features resulted in a lessening of the depression in nine patients. Only one patient went home, while three were transferred to open wards. Analysis of the rating scales showed that the depressive features disappeared, to reveal underlying schizoid thought processes.

(Authors' Abstr.)

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Effect of a Cholesterol Lowering Agent on the Aged Mentally Ill

An emulsion containing pyridoxine and linoleic acid glyceride was administered postprandially in an oral dosage to ten mentally ill patients on a normal institutional diet. This medication resulted in a substantial decrease in serum cholesterol concentration in nine of the ten patients. A confirmatory study resulted in a decrease of serum cholesterol levels in four out of five of these patients. It appears that the administration of this emulsion to patients on such a diet is an effective therapy for hypercholesteremia.

(Authors' Abstr.)

Toxicology of Marsilid^{*} and Other Amine Oxidase Inhibitors

1. RO 5-0700 (1-picolinyl-2-benzyl hydrazine) and RO 5-0831 (1-benzyl-2-(5-methyl-3-isoxazolylcarbonyl) hydrazine) are more potent inhibitors of amine oxidase than is Marsilid.
2. RO 5-0700 and RO 5-0831 can potentiate the central stimulation produced by 5-hydroxytyptophan and dihydroxyphenyl-alanine and this potentiating activity is stronger than that exerted by Marsilid.
3. Toxicity measurements in various species indicate that the higher potency of RO 5-0700 and RO 5-0831 over Marsilid as inhibitors of amine oxidase does not greatly increase the toxicity. Therefore, smaller dosages of the new drugs may achieve a desirable therapeutic response with less side-effects when compared with Marsilid.

(Authors' Abstr.)

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Migraine and Seizure States in Children

A series of 55 cases of migraine in children seen in the Seizure Control Clinic has been presented. The frequency of this condition in children and its occurrence at an early age have been emphasized. The theoretical consideration of the relationship of seizure states to migraine has been discussed with the general conclusion that severe migraine attacks may be mistaken for seizures in some cases, but that in many cases the convulsive phenomena is actually simply secondary to vascular changes related to migraine.

Excellent results from treatment combining regular medications with either the barbiturates or hydantoin drug and elimination of psychological stress is reported, improvement or control being obtained in slightly more than 80 per cent. of the cases. Prognosis is therefore thought to be good in most such cases despite a severe picture of migraine, seizures and EEG abnormality when the child is first seen.

(Authors' Abstr.)

Evaluation of Two Ataractic Agents

Two drugs—prochlorperazine and benactyzine—were evaluated in separate but similar groups of patients.

Of 188 psychoneurotics and 19 schizophrenics treated with prochlorperazine, 80 per cent. showed marked or moderate improvement in their clinical syndromes. The psychoneurotic reactions, especially anxiety, responded very well to prochlorperazine, as did paranoid delusions in the schizophrenics. The patients were free of disturbing negative psychological effects while on the medication, and their ability to sleep was significantly improved. Prochlorperazine provided no serious or prolonged side-effects during one year of administration.

Of 60 psychoneurotics treated with benactyzine, 25 per cent. showed slight to moderate improvement in their clinical syndromes; the syndromes of remaining patients either remained unchanged or became worse. Severe absent-mindedness disrupted therapy in 40 patients, causing 20 of them to stop the medication voluntarily.

(Author's Abstr.)

Treatment of Depressed and Regressed Patients with Iproniazid and Reserpine

1. Additional evidence of the value of iproniazid in the treatment of depressed, hypoactive patients is presented.

2. The drug increases psychic energy and this may result in clinical worsening as well as improvement in certain types of mental disease. It does not seem to be an ataractic but can be used in combination with one.

3. The combination of iproniazid followed a week later by reserpine seems to increase the degree of activity.

4. The addition of d-amphetamine to iproniazid accelerates the action remarkably and makes the treatment much more valuable for office use.

5. A variety of other possible applications are suggested.

(Authors' Abstr.)

The Electroencephalogram of Multiple Sclerosis

The EEG findings are reported in 192 cases of multiple sclerosis who had no prior history of epilepsy. Some of these were treated by INH. INH does not influence the EEG in multiple sclerosis. EEG abnormality does not seem to relate to severity of symptoms, nor to the predominant system involved, nor to mental symptoms in multiple sclerosis. The usual abnormality is a random, irregular slowing 5 to 8 per second, diffuse and shifting, but particularly in frontal areas. One hundred and six, or 55 per cent. of the cases at some time or another showed an abnormal tracing. This is a much higher figure of abnormality than is usually reported and would seem to demonstrate the obvious—namely, that when serial electroencephalograms are made, more abnormality is found. Because of this the differential diagnostic value of one electroencephalogram in a case of multiple sclerosis seems small unless it is correlated with the clinical neurological findings.

(Authors' Abstr.)

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Trifluoperazine in Emotionally Disturbed Office Patients

This report summarizes one year's experience with trifluoperazine, a new compound to relieve anxiety, which was evaluated in 155 office patients suffering from anxiety reactions, menopausal syndrome, or functional disorders. Of those treated 71 per cent. showed marked symptomatic relief. The percentage improved was similar even in the 59 patient control group, two had not responded well to previous tranquilizers. Side-effects of drowsiness and lethargy were negligible. In fact, on trifluoperazine, patients reported that their powers of concentration and attention increased and that they experienced no diminution of drive or initiative. Response to trifluoperazine usually occurred within the first week of administration, frequently within the first 24 to 48 hours. Used in low dosages, it does not cause daytime drowsiness or inhibit normal interest and initiative. For this reason, it appears to be particularly useful in treating office patients.

(Author's Abstr.)

Parenteral Methylphenidate Hydrochloride (Ritalin) in Chronic Underactive Schizophrenics

1. The literature on methylphenidate hydrochloride (Ritalin) and its employment as a psychoanalytic drug is briefly surveyed.
2. An investigation into the use of parenteral methylphenidate hydrochloride in chronic withdrawn underactive patients using an Activity-Withdrawal Rating Scale is described.
3. The results of this investigation show that only slight overall improvement resulted except in individual cases where the improvement was more marked but transient and not reproducible.
4. Methylphenidate hydrochloride in the dosage used seems a non-toxic drug, its chief side-effect being anorexia.
5. The results are discussed and some speculations made upon the mode of action of methylphenidate hydrochloride.
6. It is suggested that this drug is worthy of further trials.

(Author's Abstr.)

Iproniazid Used in Attempted Suicide

It was concluded that:

1. There was no evidence of any liver damage as far as could be ascertained.
2. The amount of Marsilid the patient swallowed, 1,500 mg., is apparently the largest amount recorded for any one time.
3. Instead of destroying herself with the Marsilid, the drug temporarily lifted her depression.

(Author's Abstr.)

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Effects of Iproniazid on Chronic and Regressed Schizophrenics

Iproniazid was given for 8 weeks in doses of 150 mg. daily to 32 chronically ill, withdrawn, apathetic and depressed mental patients of both sexes, mostly schizophrenics. An equal number of controls received a placebo. Strict randomization and double-blind procedures were followed. Results obtained by a rating sheet showed that 20 per cent. of the

32 patients treated had shown improvement as to apathy and/or depression. Additional information was obtained from close clinical observation of the group of 14 female patients and their controls included in this study. These results can be summarized as follows:

1. The drug improved alertness, contact, and spontaneity in more than 50 per cent. of patients, and at the same time caused undue agitation in a considerable number, rendering them more aggressive, tense and irritable, and increasing their psychomotor activity.
2. Marked individual weight changes were noticed ranging from a gain of 25 pounds to a loss of 13 pounds. Weight loss occurred in those who displayed tension and agitation under the influence of the drug.
3. Reactivation of psychotic patterns was observed in a small but significant number of patients. No side reactions in the somatic area were observed.
- Iproniazid in doses of 150 mg. daily has a marked effect on a considerable number of chronically ill mental patients. The nature of this effect is complex, but therapeutically promising and requires further investigation.

(Authors' Abstr.)

Use of Hydroxyzine in Psychosis

Hydroxyzine was used in 17 cases which were studied closely over a period of six months. Generally, all patients became more interested in their surroundings and became more alert. The drug is considered safe since no side-effects, blood dyscrasias or dysfunction of the liver were encountered. Certain symptom complexes were rated and described in the paper. Hydroxyzine was exceptionally beneficial in alleviating the symptom complexes consisting of overwhelming fear, anxiety or tension and the symptoms of bizarre, autistic or delusional thinking.

In this study, one patient was discharged, one was placed on trial visit and three patients showed continued improvement. One of the improved patients had his medication discontinued and within one week had a return of symptoms. When hydroxyzine was re-prescribed, the symptoms disappeared.

Hydroxyzine has been shown to have a definite place in the treatment of psychotic patients since all these patients had been tried on other tranquilizers and other forms of treatment.

The improvement noted and the results reported have continued to date.

(Author's Abstr.)

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Basic Studies in Mongolism

Investigations on 89 mongoloid and 60 controls have indicated an elevated serum gamma globulin. This finding is statistically significant. Serum glycoprotein and serum free amino acids comparative studies showed no significant differences in the groups studied.

(Authors' Abstr.)

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Cumulative Index of Antidepressant Medications

A preliminary screening procedure was conducted over a period of 15 months in order to evaluate the effectiveness of a number of antidepressant medications. Eleven individual preparations and two drug combinations were studied. Two groups of nine patients were used as controls—the first group received no treatment and the second group was treated with electroconvulsive therapy. As a result of this investigation, β -Phenylethylhydrazine (Nardil) was selected as the most promising chemotherapeutic agent in depression.

A total of 180 patients with depressions of both endogenous and exogenous origin was treated with this drug for varying periods ranging from 30 to 60 days. This study was conducted over a period of 10 months and comprised twenty series of nine patients.

In the treatment of depression, the response to this antidepressant therapy approached the response generally obtained from electroshock therapy; 80 per cent. of patients were discharged from the hospital as recovered within 60 to 90 days following commencement of treatment with Nardil. The remaining 20 per cent. improved with supplementary medications to the extent that electroshock treatment was never required. No significant side-effects on laboratory abnormalities were encountered.

(Author's Abstr.)

Administration of Taraxein in Humans

We have described the clinical effects noted in humans when administered taraxein, a large protein molecule isolated from the blood of schizophrenics. We feel the symptoms which are produced by rapid intravenous injection of this substance to be characteristic of schizophrenia and not similar to the effects obtained from injection of positive control substances such as bulboecapnine or D-LSD-25.

(Authors' Abstr.)

Evaluation of Deprol in Psychiatric Out-Patients

1. Deprol (meprobamate 400 mg. and benactyzine 1 mg) is not particularly effective in the treatment of out-patient schizophrenics at a dosage of four tablets daily for two weeks.

2. Meprobamate alone produces more overall improvement in such patients. In the author's opinion, it is superior to Deprol or benactyzine and may be used in doses of 400 to 1,600 mg. one to four times daily depending upon the acuteness and severity of the anxiety.

3. Deprol seems to have more antidepressant effect than benactyzine or meprobamate alone.

4. Deprol has no specific effect on delusions or hallucinations.

5. In dosages of one tablet four times a day, Deprol has no consistent side-effects but does produce occasional drowsiness.

6. Drug studies such as this are replete with pitfalls. Patients with a good prognosis may easily be selected. Double-blind techniques are not a guaranteed safeguard against bias. Statistics based upon numbers which have no basis in any unit of measurement are of questionable validity.

(Author's Abstr.)

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Clarification of the Action of Successful Treatment in the Depressions

Taking into consideration only such types of depression as called by the author affective and endogenous, a research design was established to determine if organic drastic therapy beneficially influenced such conditions by their symbolic apperception or through biological action. "Mock" E.C.T. and transorbital leucotomies were compared in results to real surgery and electrocoma applications, under strictly controlled conditions, and the results showed no effect from the "mock" treatments and excellent results from the actual ones.

The action of E.C.T., psychosurgery and the phrenopraxic drugs was studied and it was concluded that they act by lowering to normal exacerbated psychocerebral centres whose overactivity inhibits associative and conative, in addition to affective, areas, thus inducing depression.

An analysis of the results obtained with all the above methods of treatment, their mutual comparison, and their further comparison with the results obtained with analeptic and special central stimulants of the coca type, brought out the fact that three elements are involved in depressions of the types described; effective and conative inhibition, motivational inhibition and psychomotor inhibition. All the successful antidepressant treatments studied act on one or two of the inhibited areas, but not all three except indirectly. The complete anti-depressant has not yet been produced.

(Author's Abstr.)

CO₂ Therapy in Broad Spectrum Psychiatric Treatment

Carbon dioxide therapy (CDT) has an important place in office psychiatric treatment of mild psychoneurotics, but it must be used with discrimination or adverse reactions and wasted efforts result. CDT should not be used unless the physician also has facilities for giving E.C.T. because CDT can bring out a latent endogenous depression which may lead to suicide if the warnings are overlooked and appropriate supervision and E.C.T. treatment are not instituted. Non-coma carbon dioxide treatments (CDTnc) are useful in clearing repressed material from the upper layers of the unconscious mind so that coma treatments result in less violent reactions. CDT is an abreactive therapy which is mainly useful as an adjunct to intensive psychotherapy of a type which the author calls psychopenetration. CDT is dangerous in endogenous depressions, may cause the patient to interrupt prematurely therapy if over-reactions are permitted, and is futile in the treatment of established schizophrenics and psychopaths. It sometimes is useful in the final reconstruction phase of the successful treatment of schizophrenics and of severe schizoid neurotics. Theories regarding dissociation were discussed.

(Author's Abstr.)

Effect of Phenothiazine Derivatives on Liver Function

In 60 psychiatric patients with weekly controls and another 55 patients less carefully studied during therapy with different phenothiazine derivatives (chlorpromazine; KS 75-, KS 33-, TP 21-Sandoz) transient and slight liver cell dysfunction was observed in about one-fifth of the patients receiving chlorpromazine and KS 75. In addition in both of these drugs the cholestatic reaction was observed. A possible relation of the two mechanisms of liver dysfunction is discussed and the literature is reviewed. More consideration should be given to the potential liver toxicity of phenothiazine derivatives when new derivatives are used in therapy.

(Author's Abstr.)

Histopathologic Findings in the Liver and C.N.S. Following Administration of Tranquilizing Drugs

On the basis of the review of the literature as well as on the basis of the authors' own material it appears that:

1. The liver dysfunctions are frequently associated with structural changes caused by biliary stasis of an obstructive variety. The clinical and pathologic findings are generally mild, transitory and reversible in character, thus indicating a possible relationship to idiosyncrasy or constitutional predisposition. The severity of the dysfunction and the pathologic findings

appear frequently to be related to pre-existing abnormalities of the hepato-biliary tract or to the existence of other disease processes which might have an effect on the liver.

2. The adverse neurological reactions are represented predominantly by extrapyramidal symptoms followed in order of decreasing frequency by epileptiform seizures and dystonic-like symptoms. The frequency and intensity of epileptiform attacks appears to be related also to predisposing factors (questionable history of previous epileptiform manifestations, post-lobotomy, and associated with E.C.T. treatment).

3. Definite conclusions concerning characteristic structural alterations as the basis for the observed neurological complications cannot be drawn from the neuropathologically studied cases reported in the literature (3 cases) or from the authors' own personally studied 10 cases because their number is too small when compared to the number of discussed complications and because these cases appear to be associated with other pathological processes which could have conceivably masked or intensified whatever changes were present. However, the structural alterations of the basal ganglia, some hypothalamic and mesencephalic structures observed in some of the human cases may possibly be the result of a neurotropic activity of the studied tranquilizing drugs.

4. The liver dysfunction, agranulocytosis, and neurological complications appear in general not to be related to dosage, duration of treatment or age. Generally they were mild, transitory and reversible in character. In the majority of cases clinical recovery followed upon decrease or interruption of drug therapy.

5. The increased severity of the above discussed complications, in certain predisposed individuals strongly militates against indiscriminate use of these drugs.

(Authors' Abstr.)

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Treatment of Depressive States in Office Practice

Deprol was used in the treatment of 77 ambulatory depressed patients in private office practice. Two psychiatrists and two internists participated. Maximum dosage used was one tablet four times daily and average duration of treatment was five weeks.

The drug was effective in the treatment of depression. Best results were obtained in neurotic depressions in which 85 per cent. of the patients were improved to some extent by the medication, and 64 per cent. almost completely recovered. In psychotic depressions 53 per cent. showed some improvement, 21 per cent. improved to a measurable degree.

When compared with stimulant drugs or other antidepressant medications used for the same patients, Deprol was found to produce greater improvement in 61 per cent., comparable improvement in 27 per cent., and less improvement in 12 per cent.

The cardinal symptoms of depression—psychomotor retardation, self-reproach, insomnia and anorexia—were all favourably influenced by Deprol. In neurotic patients, suicidal thoughts were strikingly counteracted. Doctor-patient rapport was better and psychotherapy was facilitated by the use of Deprol when this was part of the treatment.

Important benefits of treatment noted were: (1) prompt action; (2) unimportant side-effects; (3) lessened insomnia; (4) no loss of appetite; (5) no liver dysfunction; (6) or other toxic symptoms requiring constant surveillance and laboratory tests.

(Authors' Abstr.)

Deanol: A Clinical Trial

The results indicate that about one-fourth of psychiatric outpatients with depression show improvement of this symptom after one month of treatment with deanol. This improvement was more marked in the psychotic patients who were depressed than in the depressed neurotics. A control group would be necessary in order to compare this with a spontaneous remission rate in similar depressed patients. These results can be compared to the remission rate of 23 per cent. in depressions found by Gottlieb using amobarbital and amphetamine, and to the 40 per cent. remission rate with iproniazid therapy of depression reported by Cook. This clinical evaluation indicates that deanol may be worth a trial of at least four weeks, particularly for depression with insomnia in psychotic patients.

(Authors' Abstr.)

Preliminary Study of Isocarboxazid, an Iproniazid Analog

1. Ro 5-0831/1 was given in a mean dosage of 30 mg. daily to a group of depressed hospitalized patients; 11 showed maximal improvement, seven moderate, and three minimal; five were unimproved and four worse.

2. It was given in mean dosage of 60 mg. daily to 21 extremely regressed patients. Two of these patients obtained maximal psychiatric improvement and seven others showed varying degrees of "psychic energization".

3. Seven schizophrenics, chronic but not extremely regressed, were given Ro 5-0831/1. Two improved maximally, one moderately, and one minimally. One was unchanged and two became worse.

4. Hypotension plus vertigo occurred in five patients of the 58. Three patients were taken off the medication due to this difficulty. Other patients were able to tolerate the drug despite side-effects. Four patients had extrapyramidal-like symptoms. Two cases had edema temporarily. Side-effects were less frequent among the vegetative patients on 60 mg. daily than among the depressed patients on a mean dose of 30 mg. daily.

(Authors' Abstr.)

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An Assessment of the Value of Sleep-Electroencephalography for the Diagnosis of Temporal Lobe Epilepsy

1. The diagnostic importance of sleep electroencephalography for the EEG diagnosis of temporal lobe epilepsy was studied in two groups of patients. Group I consisted of 228 temporal lobe epileptics who underwent temporal lobectomy for their seizures. Group II represents a sample of 100 patients who gave a typical history of temporal lobe attacks, but were not subjected to surgical therapy.

2. In Group I the EEG diagnosis of temporal lobe epilepsy was made without sleep in 94.3 per cent. of the cases. In Group II the EEG diagnosis of temporal lobe epilepsy was made in 72 out of the total number of 100 patients. In Group II sleep was only necessary for the diagnosis in 6.9 per cent. of the 72 patients in whom a positive EEG diagnosis of temporal

lobe epilepsy could be made. Out of 25 cases in whom no clear EEG diagnosis was made 10 had sleep records taken with negative results.

3. Among the 77 patients of Groups I and II in whom sleep records were obtained 44 showed more active epileptic discharge during sleep, whereas 23 showed no such activating effect or even some reduction of epileptiform abnormality during sleep.

4. Patients with a history of nocturnal attacks are more likely than others to require sleep activation to bring out the epileptiform abnormality, although even in this group the number of cases in which the diagnosis can be made from the waking record is still high. The higher incidence of cases in which sleep is necessary for the EEG-diagnosis among patients giving a history of nocturnal attacks is statistically significant.

5. No statistically significant difference was found between natural and drug-induced sleep with regard to their propensity to activate temporal lobe abnormalities.

6. It seems that electrocorticograms taken in temporal lobe epileptics during general anesthesia tend to show less clear diagnostic signs than those taken under local anesthesia.

7. The pathological lesions found in patients whose temporal lobe EEG abnormalities were activated by sleep and those found in patients where no such activation occurred show the same relative incidence of atrophic versus space-occupying lesions.

8. The main conclusion drawn from these findings is that although sleep tends to activate the temporal lobe epileptiform abnormality in a majority of cases, sleep electroencephalography need not be carried out as a routine procedure in patients giving a history of temporal lobe seizures, since in more than 90 per cent. of the cases in which a positive EEG diagnosis can be made this diagnosis can be established in the waking record.

(Authors' Abstr.)

Electroencephalographic Changes in Man During Use and Withdrawal of Barbiturates in Moderate Dosage

1. In contrast to doses of over 0.6 g. per day, the withdrawal of 0.4 g. daily of secobarbital or pentobarbital after three months was not followed by psychotic or convulsive manifestations in any of 18 non-epileptic subjects.

2. Seven of 13 individuals demonstrated some evidence of EEG tolerance to 0.4 g. daily of secobarbital or pentobarbital during 90 days.

3. During withdrawal from this same barbiturate regimen, 5 of 18 subjects developed paroxysmal EEG discharges which later disappeared and were not associated with observable clinical abnormalities.

(Authors' Abstr.)

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The Relationship of Epilepsy to Breech Delivery

In a group of 92 patients with epilepsy whose EEG's revealed diffusely distributed, bilaterally synchronous, spike and slow wave discharges the proportion of breech born individuals (19·6 per cent.) was found to be significantly greater than the proportion of breech birth (3·4 per cent.) in the general population. In contrast, the proportion of breech born individuals (2·8 per cent.) in a group of epileptic patients with localized EEG disturbances did not differ significantly from that in the general population. The proportion of breech born in a group of 20 patients who had petit mal seizures and also in a group of 20 patients with "classical spike and wave" was significantly greater than that in the general population. The high incidence of breech birth in patients who have epilepsy of the type associated with bilaterally synchronous spike and wave EEG disturbances strongly suggests that breech delivery is an important factor in the pathogenesis of this disorder. Breech delivery does not appear to be an important factor in the origin of focal cerebral seizures.

(Author's Abstr.)

Effects of Lesions of the Rostral Thalamus on Brain Waves and Behaviour in Cats

The EEG and behavioural effects following rostral thalamic lesions were studied in 14 cats; 3 with complete transection, 5 with complete electrolytic lesions, and 6 with partial destruction.

Behavioural effects following either complete transection or complete destruction of the rostral thalamus were similar in quality, but different in the degree of severity. The signs and symptoms were: spasticity, difficulty in walking and swallowing, reduced motility and reactivity, catatonic reaction, tendency to stick the head in a corner, and so on. These changes could last from 2 to 8 weeks. The only residual effects were some spasticity of the legs and a slight increase of docility. Cats with rostral thalamic destruction could learn a visual form discrimination.

EEG effects following either complete transection or complete destruction of the rostral thalamus were again similar in quality but different in the degree of severity. (a) The arousal pattern could be elicited within from 3 to 25 days after surgery. As shown by 3 cats with massive lesions, EEG arousal could be absent during behavioural arousal. (b) The sleep spindles were either absent throughout the post-operative survival period or might have recovered to some slight extent within 3 (transection lesion) or 5 (electrolytic lesion) months. (c) Both barbiturate bursts and recruiting responses were seen to be affected at the terminal experiment, i.e. restricted to localized cortical areas and poorly organized in form.

Partial damage to the rostral thalamus caused only transient and slight behavioural and EEG changes in the immediate post-operative period.

The results are discussed in relation to the thalamic role in behaviour and the functional significance of the final common path from the thalamic diffuse projection system to the cortex.

(Authors' Abstr.)

Electrocortical Manifestations of Epilepsy in Monkey

1. Studies were made on the local cortical potentials evoked in different areas of the monkey brain. These potentials appeared as predominantly surface-negative waves, and consistent patterns in the appearance and amplitude of the responses were exhibited by each area studied. Maximal voltages characterized the "motor area", while minimal deflections were found in the prefrontal and occipital cortex, intermediate values were present in other areas.

2. Correlation was found to exist between the excitability of cortical loci to single-shock stimuli as manifested by local cortical responses and to high-frequency stimulation as indicated by seizure after discharges.

3. When enhanced epileptogenesis was induced in a locus of the motor region by chronically circumsecting an area of cortex in a mirror site on the opposite hemisphere, increased responsiveness to single shocks was observed in the remote cortical locus. This epileptogenic effect was not due to tonic influences from the circumsected area since its excision or procainization or callosal section did not alter the augmented response.

4. The concept of dendritic depolarization as an index of neuronal excitability was discussed in relation to observed variations in the local cortical response. It was proposed that this concept could conceivably be extended to account for differences in seizure susceptibility exhibited by various cortical regions.

(Authors' Abstr.)

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A Behavioral Study of the Functions of the Rolandic Cortex in the Monkey

The experiments reported were designed to study the functional role of the precentral and postcentral gyri with special reference to somatic sensation. Six monkeys were studied neurologically and while they performed visual and somesthetic discrimination tasks. The somesthetic tasks were performed in darkness and the animals were observed with an infra-red television device.

Ablation of somatic receiving areas I and II resulted in a severe tactile defect in the limbs contralateral to the lesion, but a simple somesthetic form discrimination task was relearned after unilateral and bilateral ablation. The ability of the animals to perform this task together with the presence of a "grasp reflex" and a form of cutaneous placing reaction suggests that some form of cutaneous sensation remains after ablation.

Ablations of the precentral agranular cortex result in a temporary sensory defect detected by the initial loss of the "instinctive grasp" and tactile placing reactions, but the somesthetic form discrimination was performed without deficit.

Unilateral ablations of the combined precentral and postcentral arm area resulted in a severe sensory loss in the contralateral arm and the two animals studied were unable to perform the somesthetic discrimination task with the affected limb although a visual discrimination task was readily performed.

These findings suggest that the precentral gyrus subserves somesthesia in the absence of the postcentral gyrus. The relation of these findings to the character of the precentral afferent projection and to the functional differences between the precentral and postcentral gyri are discussed.

Analysis of the retrograde thalamic degeneration in the brains of the animals reported here, suggests that the granular tactile receiving area is the essential projection field of the ventro-basal (tactile) complex of the thalamus. Observations on the effect of Rolandic lesions on motor function are also presented.

(Authors' Abstr.)

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Projection of the Gracile and Cuneate Nuclei in Macaca mulatta: An Experimental Degeneration Study

1. Following lesions to the gracile and cuneate nuclei in three monkeys, axon degeneration was traced by the method of Nauta.

2. The efferent fibres from these nuclei were found to decussate completely, and to terminate almost exclusively in the nucleus ventralis posterolateralis thalami.

3. A small amount of terminal degeneration was seen in the n. paralemniscalis, embedded in the medial lemniscus in the mesencephalon.

4. No terminal degeneration was found in the brain stem reticular formation, or in nuclei of the extrapyramidal motor system.

5. The significance of these findings is discussed with particular reference to:

1. The extrapyramidal motor system.

2. Lateralization of sensory representation.

3. The nature of afferent impulses to the brain stem reticular formation.

(Author's Abstr.)

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Some Projections from the Peri-central Cortex to the Pons and Lower Brain Stem in Monkey and Chimpanzee

In monkeys, using the Nauta-Gygax silver technique, cortico-bulbar fibres were found to distribute to the motor nuclei, the spinal trigeminal complex, and adjacent lateral tegmentum. The origin of these projections appeared to be the following:

The fibres to the motor nuclei originate primarily in the posterior parts of the pre-central gyrus (face area), while the fibres to the lateral tegmentum exhibit a more diffuse pre-central origin. In the chimpanzee, in contrast to the monkey, the posterior parts of the pre-central gyrus (face area; approximately area 4) project almost exclusively to the motor nuclei, while the fibres to the lateral tegmentum originate from rostrally adjacent cortical areas, together with additional fibres to the motor nuclei. It was inferred that the fibres to the lateral tegmentum represent an "indirect" cortico-nuclear projection.

The cortical fibres to the spinal trigeminal complex originate primarily in the post-central gyrus. This gyrus also distributes fibres to the posterior horn of the spinal cord (nucleus proprius) as well as to the region of the nuclei cuneatus and gracilis. The latter projection has an additional origin in the pre-central gyrus.

(Author's Abstr.)

Responses to Electrical Stimulation of the Cerebellum of Unanesthetized Birds

1. Selected loci in the cerebellum have been stimulated in a series of 40 chickens and three pigeons.
2. The responses observed can be divided into three phases—stimulus, rebound and long after-effect.
3. Every bird stimulated responded by swaying or rotating and squatting (flexion of antigravity muscles).
4. Appendicular responses associated with balancing were noted and compared with like responses observed in a normal animal.
5. Head turning was observed in all cases except when the stimulating electrode was on the midline. Simple ipsilateral turning only followed stimulation of all areas except the region of centralis and culmen. Stimulation of points in these regions but not on the midline gave mixed head turning responses.
6. Neck movements were elicited from all areas stimulated, but the pattern of responses varied from folium to folium. Extension of the neck musculature was obtained from centralis, folium IV of culmen, declive, and uvula. Retraction was obtained from folium Vb of culmen and tuber; mixed responses were obtained from folium Va of the culmen and from the pyramis.
7. Movements of the beak, tongue or nictitating membranes were recorded from centralis, declive, tuber and pyramis.
8. The pyramis was the most consistent source of discrete wing movements. Other areas, Va of culmen, VIa+b of declive, and pyramis also gave wing movements that were not associated with balancing.
9. Centralis, IV of culmen, and uvula gave precise stimulatory and rebound movements of the tail.
10. Birds stimulated in areas posterior to the fissura secunda had a hyperactive long after-effect; those stimulated in other regions of the cerebellum showed a period of quiescence which in some instances was interrupted by a period of activity.
11. Three pigeons stimulated while flying required a greater intensity of current to produce a response than was needed while they were standing or walking.
12. Under comparable conditions to those of the chicken, stimulation of the pigeon's cerebellum gave similar responses, i.e. homolateral head turning, tilting, and flexion of leg muscles. The rebound phase of head turning, while the animal was walking or standing, was observed in every case.

(Author's Abstr.)

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A Life-table for Mongols With the Causes of Death

A life-table has been prepared for nearly 700 mongol children attending The Hospital for Sick Children between 1944 and 1955. This indicates that of live-born mongols thirty per cent. are dead by the age of one month, fifty-three per cent. by one year and sixty per cent. by the age of ten years. The findings are in good agreement with a series from Birmingham born between 1942 and 1952. It is confirmed that the sex-ratio for mongolism increases with age and is probably already high at birth. A comparison of the mortality for those attending from 1944 to 1948 and from 1949 to 1955 suggests that the mortality has decreased by forty per cent. in the later period.

An increase in the survival rate of mongols is confirmed by estimates of the incidence of mongolism in the population at age ten. Figures supplied by the Medical Officers of Health for London and the Home Counties indicate that this incidence in 1958 is a little over one in 1,000. Compared with earlier estimates this indicates that the incidence of mongolism at age ten has doubled since 1949 and doubled again since 1929. The fall in mortality for mongols is of the same order as, though a little less than, that for children in general.

Comparing the life-tables with the estimates of survival for incidence of mongolism among live-births and at age ten shows fair agreement for earlier years, but the most recent population figures suggest that the mortality between birth and ten years is only about 340 per thousand. This indicates either that the true incidence of mongolism among live-births is more than the estimated figure of 1.6 per thousand, or that the life-tables are over-estimating the mortality in recent years.

The causes of the 136 deaths in the series are analysed. The major causes are bronchopneumonia and congenital heart disease. The association of mongolism and leukaemia in childhood is confirmed and attention drawn to an association between mongolism and Hirschsprung's disease.

(Author's Abstr.)

The Polymorphonuclear Lobe Count in Mongolism and Its Relation to the Total Leucocyte Count

The number of lobes per nucleus of the polymorphonuclear neutrophil leucocytes have been counted in fifty children with mongolism and fifty non-mongol mentally defective children of the same age group. By relating the polymorphonuclear cell lobe count to the total leucocyte count and to the neutrophil count, it was found that for any constant total leucocyte or neutrophil count the polymorphonuclear count of the mongols was lower than that of the controls.

The lobe count was unaffected by age.

It is concluded that infections are unlikely to account for the lowered lobe count of mongols.

(Author's Abstr.)

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Psychological Studies of Korsakoff's Psychosis: II. Perceptual Functions

A battery of psychological experiments exploring various perceptual processes, shows that the cognitive disturbance in Korsakoff's psychosis is neither exclusively, nor primarily in memorizing or learning. Patients suffering from this disease, even when capable of rational

behaviour and immune from confusional and confabulatory symptoms, are markedly defective in their perceptual functioning. Comparing them with controls drawn from psychiatric patients in an alcoholic clinic and from hospitalized neurological patients not diagnosed as brain-damaged or as alcoholic, the Korsakoff patients show a deficit on most perceptual tests. A notable exception to this observation are tasks which depend on the immediate apprehension of spatially and temporally unitary patterns or situations. The several discrete findings of this study can be subsumed most satisfactorily under a common principle by thinking of the Korsakoff patient as limited in his capacity to sustain more than a single perceptual set or attitude at a time, or to alter his orientation while the sensory input continues to confirm an expectancy he has adopted. This dependance on one aspect of the stimulus situation prevents him from integrating experiences, which may be the cause of his inability to learn or recall them; it also deprives him of those constant checking operations the absence of which has been proposed as an explanation of confabulatory behaviour. The perceptual disorder appears to be a primary factor in the mental syndrome characteristic of Korsakoff's psychosis; though indeed it may jointly with other cognitive defects manifest a common underlying attitudinal impairment.

(Author's Abstr.)

Investigations of the Urinary Excretion Pattern in Psychotic Patients

Chromatographic analysis of urines of 21 psychotic patients for urinary indoles revealed the presence in the majority of schizophrenics of an unknown compound, which was absent from the majority of urines of non-schizophrenic mental patients.

The urines of psychotics showed on chromatographic analysis for amino acids and in the "Fluorindal reaction" no significant abnormalities.

A modification of the standard glyoxylic acid test is described. The results of the test with urines of 128 psychotic patients are evaluated. It is concluded that the modified test confirmed results previously obtained in the positive range, increased the number of negative tests with schizophrenics and added to the sensitivity of the test. It also improved the clarity of the test colours.

The effect of treatment of urines with hydrogen peroxide on the glyoxylic acid test was studied and it was found that the oxidizer eliminates the interference of non-indolic substances with the test. The effect of some organic non-psychotic disorders on the test results is noted and the implication discussed.

(Author's Abstr.)

Clinical and Pharmacological Studies of Marsilid and Theoretical Considerations Concerning Its Antidepressant Action

1. Marsilid is an antidepressant agent and is active in psychogenic depressions, in depressions caused by chronic physical illness, and in so-called psychosomatic disorders. This drug action suggests the possibility of a common pathological denominator in all these conditions.

2. The following three stages are typical of Marsilid therapy: (a) Lessening of tension, depression and accompanying symptoms; (b) well-being, increase of interests and energy; (c) elation, overactivity and shallow affect. This pharmacodynamic process may occur in the treatment or post-treatment period.

3. An attempt was made to offer a comprehensive interpretation of Marsilid action. It was hypothesized: (a) that certain autonomic and affective reactions are the result of a specific action on subcortical centres; (b) that behavioural and affective changes are related to an increased input of sensations.

4. The use of the drug is limited by its toxicity, its widespread action on the brain and by the difficulty of achieving a satisfactory psychophysiological homeostasis.

5. It was hypothesized that the drug's value lies in its ability to correct neurohumoral imbalance. Due to this action the effect of Marsilid on depressions and allied conditions is corrective and not symptomatic.

(Author's Abstr.)

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Pharmacological Reduction of Abnormality in Multiple Sclerosis Within Minutes: A Statistical Study

1. A statistical study is reported of the phenomenon of pharmacological reduction of abnormality within minutes (PRA) in multiple sclerosis (this was previously termed "relief by flush"). This phenomenon is the reduction within an hour or (usually) less, of neural deficits in multiple sclerosis, after the administration of certain drugs.

2. It is the phenomenon itself which is of major interest, and not its therapeutic application. In studying a patient, the essential thing is to learn whether the phenomenon can or cannot be demonstrated in relation to one or more specific symptoms, regardless of whether it is transient or permanent in duration, and regardless of any possible therapeutic utility.

3. Neural deficits of every type are equally affected.

4. The drugs chiefly employed have been histamine diphosphate, carbon dioxide and amyl nitrite, which have in common the production of intracranial vasodilatation, and Hydergine (Sandoz).

5. The study is of 4,458 separate observations, on 311 symptoms in 116 patients.

6. The producibility of PRA and the length of time it lasts are largely dependent on the prior duration of the symptoms involved. With symptoms of brief prior duration, PRA is much more likely to occur with predictable regularity, to be marked and to be enduring, than with symptoms of long prior duration. Extensive neural damage residual from earlier attacks reduces the chances of occurrence of the phenomenon.

7. The incidence of PRA is far greater than that of spontaneous remissions, according to a comparison with the data of Kurtzke concerning spontaneous remissions.

8. The phenomenon is not dependent on spontaneous remissions, psychological factors, nor rest, as attested by control data.

9. The phenomenon often lends itself to therapeutic uses. The same control methods used for the phenomenon itself in excluding psychological, rest and spontaneous remission factors, are employable here.

10. In many cases a lasting effect follows a single drug administration. This is regarded as a demonstration of the phenomenon, and of its therapeutic applicability in "pure form". It means that the indicated symptoms ran an unchanged course from their onset until a few minutes after the first or other early drug administration, at which time a lasting change occurred.

(Author's Abstr.)

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Tumors of the Septum Pellucidum and Adjacent Structures with Abnormal Affective Behavior: An Anterior Midline Structure Syndrome

The hypothesis correlating neoplasia affecting the septum pellucidum and the adjacent structures with abnormal affective behaviour has been strengthened by further clinical observations. In addition, the modern concepts of the mechanism of emotion both from an anatomical and a physiological point of view seem to support this hypothesis. In the authors' own study they attempted to explore the problem of the degree to which a neoplasm will produce behavioural changes similar to those which follow electrolytic lesions. Although the technique was only partially successful, it was found that tumor and experimental lesions produced strikingly similar behavioural results. In addition, the notion that mechanisms associated with expansion of the tumor are sufficient to interfere with normal functioning of the structures involved was given support. It appears reasonable to conclude that a clinical syndrome of hyperemotionality may be associated with tumors of the anterior midline structures, more specifically of the septum pellucidum and fornix.

(Authors' Abstr.)

The Application of Triiodothyronine in the Treatment of Mental Disorders

It sometimes happens in a psychiatric service that patients with hypometabolism are treated symptomatically for depression, while their thyroidal metabolic state is overlooked. It is understandable that this should occur since the general lassitude, irritability, somnolence and decreased mental alertness which often accompany hypometabolism may be the major complaints of the patient and the reason he is brought to the attention of the psychiatrist. In the ten patients here described, for example, these psychic symptoms predominated. An empirical trial with Lio-thyronine quickly brought about an improvement in their condition. The good responses may have resulted from a correction of a hypometabolic state showing symptoms common to both the depressive and the hypometabolic condition. Of the ten patients, only two remained in the hospital. Of the 24 patients treated with Cytomel during the period from September, 1956 to September, 1957, 17 were discharged and the majority of the remainder are improved. Of the 17 discharged patients, 15 remained out of the hospital one year or more after discharge. Since Lio-thyronine acts more quickly than Thyroxine, is absorbed and eliminated more quickly and its activity is much more potent than Thyroxine's (6), it is superior to desiccated thyroid or L-thyroxine for empirical trial in psychiatry. In the doses used no untoward effects were encountered during and after the trial.

(Author's Abstr.)

Some Effects of a New Psychotogen in Depressive States

A new anticholinergic psychotomimetic agent, N-ethyl-3-piperidyl cyclopentylphenyl glycolate (JB-329), has been used in the treatment of a small number of depressed patients. The drug induces a drive of activity accompanied by some mood elevation. This seemingly desirable effect from a therapist's viewpoint occurs after a period in which there are psychopathological effects of a definitely psychotic nature. The post-psychotic effects which seem desirable are of a prolonged duration (days to weeks possibly). There is at least slight evidence in two cases of a continuing state of improved integration of the mental functioning and behaviour.

(Authors' Abstr.)

The Use of Doxylamine in Schizophrenia: Pitfalls in the Evaluation of a New Drug

Doxylamine, used previously as an antihistamine, was given to a small number of chronic psychotic patients at a state hospital. The experimental study was of three months duration and doses up to 900 mg. per day were administered. A double blind technique was used, one-half the patients receiving a placebo. Seventy per cent. of the Doxylamine patients and fifty-three per cent. of the placebo patients remained unimproved. Side-effects were virtually non-existent; one patient on the drug had an acute hypotensive reaction.

A plea is made for the adoption of double blind placebo techniques in the evaluation of drugs used in treating the mentally ill.

(Authors' Abstr.)

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Pharmacological Selectivity Manifested by Agents Acting Upon the Cortical Dendritic

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The Adrenochrome Model and Schizophrenia

Model psychoses and schizophrenia have been compared using four different experimental methods which assume that there is a major biochemical abnormality in this illness.

First, it is now possible to discriminate between schizophrenic groups and others on the basis of several biological and biochemical assays which indicate the presence of unusual biochemical substances in schizophrenic blood and urine. The adrenochrome hypothesis predicts that these differences ought to be present and may lead to the discovery of specific schizophrenic metabolites arising from adrenochrome.

Second, adrenochrome and adrenolutin produce psychological changes in normals which reproduce some of the findings in schizophrenia. Third, phosphate excretion is altered by both adrenolutin and LSD-25 in a way which resembles the excretion in schizophrenics and not that in anxiety. Substances which antagonize psychotomimetics tend to be therapeutic for schizophrenia whereas substances which potentiate are not. Finally, treatments based on the adrenochrome hypothesis have shown some therapeutic success for early schizophrenic patients.

The evidence presented shows that schizophrenia and the model psychosis have many more similarities than differences and that the adrenochrome hypothesis is a useful model for schizophrenia which may be useful in developing better models.

(Authors' Abstr.)

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Psychological Studies of Korsakoff's Psychosis: III. Concept Formation

The performance of 24 Korsakoff patients, studied in the chronic phase of the illness by means of a series of experiments, and tested against controls drawn from non-hospitalized alcoholic and hospitalized neurological patients, has demonstrated three major sources of their deficiency in concept formation. Categories the Korsakoff patients use for classification are looser than those applied by the controls. Korsakoff patients are virtually incapable of discovering the appropriate criteria of categorization if these happen to be different from attributes familiar and therefore first resorted to; they are subject to particularly severe limitations in forming sequential concepts. In addition, they often fail to apply effectively concepts which they have either discovered for themselves or been told, and have grasped and retained in memory. These defects in concept formation are neither explained by the well-known memory impairment in Korsakoff's psychosis, nor entirely by perceptual deficiencies, but appear to be additional to the latter. The defects in perception and concept formation which characterize the Korsakoff syndrome show many parallel characteristics, and suggest dysfunctioning in common basic processes, such as set rigidity, i.e. inability to adopt new attitudes of orientation to a situation. The resultant failure to order and integrate experiences could itself be a cause of the more familiar symptoms of memory disturbance.

(Author's Abstr.)

Studies on Serum Oxidase (Ceruloplasmin) Inhibition by Tryptophan Metabolites

Of the thirteen tryptophan metabolites studied to date, serotonin, 5-hydroxytryptophan, 5-hydroxyindole-3-acetic acid, bufotenine and 3-hydroxyanthranilic acid were capable of inhibiting the oxidation of N,N-dimethyl-p-phenylenediamine by purified ceruloplasmin and serum oxidase. Two types of inhibition were noted and discussed.

(Authors' Abstr.)

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Endocrine and Metabolic Conditions Related to Pathology in the Hypothalamus: A Review

The clinical case material of 100 patients, with hypothalamic pathology selected from the literature, has been surveyed. In the great majority of these cases autopsy or at least surgical evidence of hypothalamic invasion by neoplasm or other pathology was available. The effect of such hypothalamic pathology in water metabolism, electrolyte balance and release of trophic hormones from the adenohipophysis has been discussed. Experimental evidence and clinical findings in these cases have been compared in regard to each of these individual phases of hypothalamic control. As far as the effect of disturbed hypothalamic functions on the target organs is concerned the gonads appeared to be most strongly impaired, the thyroid slightly and the adrenal cortices least. Disturbances, of water metabolism, mainly diabetes insipidus, occurred in direct proportion to the destruction of the commonly accepted control centres. However, in a group of 30 patients with severe traumatic brain lesions and marked hyper-tonicity of the blood the question of impairment of other centres regulating electrolyte balance, as suggested in animal experimentation, was raised. Another group of seven patients with hypothalamic pathology and disturbed blood-protein levels has also been discussed.

(Author's Abstr.)

Serum Magnesium in Delirium Tremens and Alcoholic Hallucinoses

Serum magnesium was studied in 30 patients with delirium tremens, 20 patients with alcoholic hallucinosis, and 18 controls. Group values were significantly low in alcoholic hallucinosis and still lower in delirium tremens. Individual values had a narrow distribution in the controls and a significantly wider distribution in alcoholic hallucinosis and delirium tremens. Seven of the delirium tremens patients were studied during convalescence; the value of serum magnesium increased in each without the use of magnesium in the therapy.

These findings are discussed in relationship to the literature on magnesium in alcoholic withdrawal states and to the role of magnesium in physiological processes.

(Authors' Abstr.)

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The Effect of Age on the Non-Haemin Iron in the Human Brain

1. The content of non-haemin iron in different parts of the human brain has been determined from birth to old age. The highest iron values were found in the structures of the extrapyramidal system.

2. The distribution of the non-haemin iron in the cerebral cortex shows a characteristic pattern. The highest concentrations were found in the motor cortex, followed by occipital, sensory and parietal cortex. The lowest figures were found for the prefrontal and temporal cortex.

3. An increase in non-haemin iron occurs with advancing age in all regions of the brain examined except in the medulla oblongata. The rise in iron values is rapid during the first two decades of life, then more gradual. There are some differences in the slopes of the curves for the structures investigated.

4. The quantity of non-haemin iron in the brain is to a large extent independent of the iron stores in the body.

5. A parallel is found between iron content and phylogenetic age of the structures investigated.

6. The histological estimations of the amount of iron in the extrapyramidal centres agree fairly well with the chemical determinations. In the cerebral cortex histologically demonstrable iron could not be found in young and middle-aged individuals. After the age of about 65 minimal iron deposits were detected in the motor and occipital cortex. No microscopically visible iron was found in the white matter.

7. About one-third of the non-haemin iron of the brain can be extracted by buffer solutions. This iron is bound to a protein which seems to be similar to ferritin. It is assumed that this iron-rich protein is a store of iron reserved for the needs of the brain.

8. A high concentration of non-haemin iron is found in microsomes and mitochondria of dog brain.

(Authors' Abstr.)

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Comparative Histochemistry of Lipids in Relation to Myelination in Rabbit Brain

1. Histochemical techniques for phospho- and glycolipids were applied to the problem of myelination in the developing rabbit brain.

2. Myelinated fibres were first demonstrable, as early as 24 hours after birth, in the medulla oblongata. The process of myelination was histochemically completed between the second and fifth months.

3. The earlier development of myelin in the phylogenetically older parts of the brain was clearly shown.

4. Diffuse staining of the neuropil occurred in brains from 24 hours to 28 days old. This was considered to indicate temporary storage of sphingolipid prior to its incorporation in the myelin sheaths.

5. Diffuse intracellular phospholipid was especially apparent in all parts of the brain from the fifth to the seventh day. The adult pattern emerged at the twenty-eighth day. The nature and function of this lipid remain obscure.

6. The histochemical results, in general, agreed well with the findings of reported biochemical studies on similar material. In particular, the striking increase in cerebroside content of the myelin sheaths, observed biochemically at and after the ninth day, was reflected in the histochemical tests.

(Authors' Abstr.)

Changes in the Composition of the Developing Mouse Brain During Early Myelination

The developing mouse brain has been studied from 1 day to the adult stage (10 weeks) with respect to changes taking place in total lipid, total lipid-free residue, total water, total lipid phosphorus, total nucleic acids (RNA and DNA), cerebrosides and water-soluble glycolipids (gangliosides and polycerebrosides), in an effort to delineate the role played by water-soluble glycolipids in the early phases of myelination. An attempt was made to correlate these changes with the changing histological picture and the development of myelin. The data obtained have led to the following conclusions:

1. The onset of histologically evident myelination is preceded by a sharp drop in water and nucleic acid content of the brain, presumably due in part to a decrease in glial cellular elements.
 2. Although the increase in cerebrosides parallels the increase in myelination, this increase is not accompanied by a proportional net increase in other lipids, so that the bulk of myelin-lipids appears to be formed from lipids already present in brain when myelin makes its appearance and continues to increase.
 3. Water-soluble glycolipids show a steady increase until the twelfth day, and from then on maintain a relatively constant absolute level in spite of the continued growth and maturation of brain. This suggests a high rate of turnover for this group of substances.
 4. In the 1-12 day period the water-soluble glycolipid fraction is poor in neuraminic acid (polycerebrosides predominate) while from then on a relatively constant proportion of gangliosides and polycerebrosides is in evidence.
- The results are discussed in relation to the manner in which myelin may be formed, and with respect to the possible role of water-soluble glycolipids as precursors of cerebrosides.

(Authors' Abstr.)

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Amino Acid and Protein Metabolism of the Brain: IV. The Metabolism of Glutamic Acid

The metabolism of ¹⁴C-labelled glutamic acid was studied in intact rats and mice. It appears that the bulk of the administered amino acid enters brain, liver, kidney and muscle as such and not with prior conversion to the amide. The entry of ¹⁴C glutamic acid into the various organs was very rapid and within minutes the glutamic acid, glutamine, GSH fraction of the brain, liver and kidney, and the γ -aminobutyric acid fraction of brain were significantly labelled. Within 2 minutes after the administration of ¹⁴C glutamic acid the specific activity of the organ glutamine approached that of the dicarboxylic acid, a fact which indicates the rapidity of intraconversion of the glutamic acid-glutamine system.

In experiments of longer duration the specific activities of glutamic acid, glutamine, GSH, and γ -aminobutyric acid decreased as would be expected from their rapid metabolism. In a number of short time experiments the specific activity of plasma glutamine was higher than that of liver glutamic acid and glutamine. This finding is interpreted as suggesting that the amide is synthesized in a compartment of the organ (endoplasmic reticulum?) from labelled glutamic acid not diluted extensively by organ glutamic acid.

The flux of glutamic acid from the circulating blood into brain and liver is estimated. A method is presented for the efficient separation in isotope experiments of glutamic acid and its metabolic derivatives.

(Authors' Abstr.)

Selective Depletion of Noradrenaline and 5-Hydroxytryptamine from Rat Brain and Intestine by Rauwolfia Alkaloids

Raunescine, reserpine and yohimbine were injected intraperitoneally into rats and the animals were killed 4 hours after the drug administration. Both 5-hydroxytryptamine (5-HT) and noradrenaline from brain and intestinal tissue were analysed by bioassay.

In suitable doses raunescine (5 mg./kg.) and reserpine (2.5 mg./kg.) are able to deplete about 80 per cent. of the noradrenaline content as compared with a 40-55 per cent. loss of 5-HT in the brain. In the intestine this difference is very clear. Doses of 0.1 mg./kg. of reserpine and 0.5 mg./kg. of raunescine deplete most of the noradrenaline, but doses from ten to a hundred times higher do not lower the 5-HT content in this tissue by more than about 35 per cent.

Yohimbine (20-30 mg./kg.) leaves 5-HT intact in both tissues. In these doses it lowers brain noradrenaline by no more than 50 per cent. It does not reduce the noradrenaline content of intestine. Experiments carried out at elevated environmental temperatures indicate that the effect on brain noradrenaline is not due to the hypothermia that yohimbine is likely to produce at room temperature.

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The Metabolism of Cholesterol and Fatty Acids in the Central Nervous System

The incorporation of ^{14}C -methyl-labelled sodium acetate into young and adult rat brain cholesterol and fatty acids was accomplished by injecting the acetate directly into the brain, thus by-passing the blood-brain barrier. Only small or negligible amounts of ^{14}C were incorporated into these substances when the acetate was injected intraperitoneally into adult rats. On intracerebral injection non-saponifiable material not precipitated by digitonin became labelled also. ^{14}C activity in these various lipid fractions was detected as much as a year after injection.

(Authors' Abstr.)

The Liberation of Active Enzymes from Brain Tissue by Lysolecithin

1. A study has been made of the activity of various hydrolytic enzymes in brain homogenates "cleared" with lysolecithin.

2. It has been found that true and pseudo-cholinesterase, alkaline phosphatase, glycerylphosphorylcholine diesterase, proteinase and transaminase are all as active in the cleared as in control homogenates. Tributyrinase and acid phosphatase are also present, but are less active in the cleared preparations. Mono-amine oxidase is also less active.

3. Lysolecithin has also been shown to cause a rapid release of both true and pseudo-cholinesterase from brain slices.

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A Method for Studying Metabolic Pathways in the Brain of the Intact Animal. The Conversion of Proline to Other Amino Acids

Evidence that the living rat brain can convert L-proline to glutamic acid, aspartic acid, alanine, arginine, γ -aminobutyric acid and ornithine is presented. The implications of these findings with respect to: (1) previous tissue-slice experiments on amino acid oxidation in brain and (2) ammonia detoxication in brain are discussed.

(Authors' Abstr.)

The Penetration of Proline and Proline Derivatives into Brain

The penetration of blood-brain barrier by proline and N-acetylproline was found to be low, as compared to high penetration rates for proline ethyl ester and N-acetylproline ethyl ester. Intravenous injection of proline ethyl ester was also found to be effective in elevating the level of free proline within the brain. The significance of these findings with respect to the design of studies on cerebral metabolism of proline is discussed.

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Action of D-Lysergic Acid Diethylamide on Lateral Geniculate Synapses

1. The effect of LSD on the potentials associated with synaptic transmission in the lateral geniculate body in the cat have been studied by means of extracellular microelectrodes. The drug was delivered either by injection into the carotid bloodstream via the lingual artery or by intravenous injection. The potentials studied were mainly those evoked by electrical stimulation of the contralateral optic nerve.

2. LSD has no effect on the latency or amplitude of the presynaptic spike.

3. LSD depresses and, in larger doses, blocks transmission through the lateral geniculate. The effect is completely reversible and no excitatory action has been observed. The parameters of this blocking effect are described in detail.

4. The electrical records display evidence of two postsynaptic components, a local synaptic potential and a propagated action potential. LSD leads to a reduction in amplitude of the synaptic potential below the threshold for initiation of the propagated spike.

5. The repetitive discharge of the geniculate neurons caused by a large-fibre optic tract volley is depressed or completely inhibited by LSD. The amplitudes of the postsynaptic spikes are all equally depressed and recover together.

6. Small- and large-fibre synaptic activities in the lateral geniculate are equally affected by LSD.

7. Intravenous LSD in the cat under Dial anaesthesia requires about 15 times the total dose for a similar effect compared to relatively close intra-arterial injection. The onset of depression is slower and recovery more prolonged.
8. An intravenous dose of about 1 mg./kg. in the conscious cat probably causes blindness or at least marked impairment of vision with very much less effect on general bodily activities. The effect is reversible.
9. It is concluded that LSD blocks transmission through the lateral geniculate either by inhibiting the release of the transmitter substance or by competing for the receptor sites on the postsynaptic membrane.

(Authors' Abstr.)

Mechanism of Gamma Aminobutyric Acid (GABA) Action and Its Relation to Synaptic Inhibition

Mechanisms of the blocking action of gamma aminobutyric acid (GABA) were analyzed in isolated stretch receptor cells of crayfish and lobster. A striking parallelism between the effects of GABA and of neural inhibition has been found.

1. GABA in concentrations near 10^{-5} M/l. blocks afferent discharges caused by stretch deformation in slowly adapting receptor cells in the crayfish. Lobster cells as a rule require higher concentrations. It is proposed that the following general mechanisms bring about the blocking action of GABA and of the inhibitory neural transmitter. When the dendrites and cell body are depolarized by stretch, an impulse is set up in the axon near the cell body. GABA and the neural transmitter increase the conductance within the cell, thereby reducing the stretch depolarization reaching the site of impulse origin. Thus the excitatory "drive" (or "generator potential") which leads to the setting up of conducted impulses is effectively reduced or removed, although the excitatory stimulus persists. If the cell is at rest, application of GABA or inhibitory impulses need not change the membrane potential, although the inhibitory process is fully active.
2. In increasing concentrations GABA reduces and eventually abolishes the inhibitory synaptic potentials. This effect is brought about by the progressively increasing hyperpolarizing action of GABA which drives the cell membrane to an equilibrium level which is usually similar to that of the neural inhibitory transmitter process. At concentrations beyond 10-15 times threshold for block, GABA has a dual action; it first hyperpolarizes and then depolarizes the receptor cell.
3. At near threshold concentrations GABA not only reduces the inhibitory synaptic potential peak but also accelerates its falling phase. GABA has the same effect on the after-positivities of antidromic impulses. Their hyperpolarization peaks are reduced and the recovery phases are shortened. The acceleration of the time course of these potentials is interpreted as an increased conductance to specific ions in the dendrites and cell body. Concentrations even 1,000 times threshold for block do not affect axon conduction or change appreciably the axon time constants.
4. If K^{+} in the extracellular solution is reduced or absent, the hyperpolarizing action of GABA and of the neural inhibitory transmitter is increased. This parallel effect suggests a common mechanism.
5. Depending on concentration, the blocking effects decrease or disappear while GABA solution still surrounds the cells. Such a recovery is prevented if the fluid around the cell is kept stirred or is periodically replaced by a fresh solution of the same concentration. These results indicate that GABA is inactivated by the tissue. The inactivation process can be followed by registering the sensory discharge frequencies in a slowly adapting cell or by following the recovery toward normal of the after-positivities of antidromic impulses. Gamma guanidobutyric acid which also blocks discharges by a similar mechanism as GABA is not inactivated in a similar manner.
6. The site of GABA action cannot be located exactly within the cells. GABA blocks in the lobster the 7th median thoracic receptor which histologically has no inhibitory synapses. Its action, therefore, is not confined to subsynaptic inhibitory areas. It is suggested that part at least of the GABA action takes place in the large portion of dendrites and in the cell body.
7. Although GABA is found in the nervous system, the role of an inhibitory transmitter cannot be assigned to it on the basis of available evidence.

(Authors' Abstr.)

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Blood Pressure Alterations Secondary to Amygdaloid and Periamygdaloid After-Discharges

1. Amygdaloid and periamygdaloid seizures were electrically induced in a series of 46 awake and unanesthetized and three anesthetized cats.
2. Simultaneous blood pressure, electroencephalographic and behavioural changes were recorded during the electrical stimulations and after-discharges.
3. Blood pressure depression invariably occurred during the after-discharges.
4. After-discharges of short duration (20 seconds or less) were associated with greater blood pressure depressions than those of longer duration (greater than 20 seconds).
5. Amygdaloid after-discharges in the unanesthetized cat appeared to have a greater influence on depressor rather than pressor mechanisms.
6. A rise in pressure was seen only when the amygdaloid discharges propagated to closely associated structural systems such as the hippocampus and fornix.
7. The greatest degree of blood pressure depression appears to occur more frequently following stimulation in the anterior and central-medial regions of the amygdala.
8. Various behavioural changes such as altered respiration, mastication, ipsilateral facial movements, etc., did not greatly influence the blood pressure response.
9. In all but two experiments pulse rate and rhythm were unaltered by the discharge.
10. The systolic component appeared to vary more than the diastolic component during the after-discharges which displayed pulse pressure changes.
11. Pressor and depressor reactions are discussed in relation to the frequency and duration of an after-discharge.

(Authors' Abstr.)

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Afferent Projections Through Ventrolateral Funiculi to Thalamus of Cat

1. Electrical stimuli delivered to the proximal end of cut hindlimb cutaneous nerves from both limbs evoked low-amplitude responses in the lateral white matter of the spinal cord. This evoked activity persisted after section of the remainder of the spinal cord at a level between the dorsal roots of entrance of the nerve and the active locus. Electrical stimulation of the responsive spinal loci evoked potentials in the somatosensory areas of the cerebral cortex even though both dorsal funiculi had been severed several segments rostral to the stimulating electrode.
2. Cutaneous nerve stimulation evoked responses in two regions of the rostral brainstem by way of pathways traversing the ventral and lateral funiculi of the spinal cord. One of these brainstem centres comprising the well-known primary relay nuclei of the cutaneous systems, the ventrobasal complex. The other responsive zone was situated caudal and medial to the ventrobasal nuclei and corresponded largely to the posterior nuclear group of the pulvinar-posterior system, including the magnocellular division of the medial geniculate body.
3. The evoked activity recorded from the ventrobasal nuclei was initiated predominantly if not exclusively by stimulation of the contralateral cutaneous nerves employed in this study. The responsive regions within these nuclei were few in number and displayed a topographic organization similar to that reported previously for these cell groups. The latency of the evoked potentials recorded from the ventrobasal complex in cats in which chronic or subacute spinal cord sections were employed approximated that observed by others in intact animals for comparable cutaneous inputs.

4. Stimulation of cutaneous nerves in each of the four limbs evoked complex potentials in the posterior nuclear group. No clear evidence for a topographic organization of the input to this region was found. While the latencies of the evoked potentials recorded from this region generally were somewhat longer and more variable than those observed for the ventrobasal complex, some responses occurred after time delays similar to those recorded from the ventrobasal complex. Ipsilateral cutaneous nerve inputs evoked discharges in this posterior region after longer latencies than did the corresponding contralateral nerve.

5. Possible relationships of these ventrolateral pathways to the rostral brainstem and the cerebral cortex are discussed.

(Authors' Abstr.)

Differential Effects of Resections of Somatic Areas I and II in Monkeys

The performance of eight rhesus monkeys on six somesthetic discriminations (multiple cue, size plus form, form, and three degrees of roughness) were studied pre- and post-operatively. The results indicated that:

1. Animals with post-central lesions (SI) fail to retain and have marked difficulty relearning most of the tasks. This somatic disturbance was duplicated and not exacerbated by combined removals of somatic areas I and II, and Brodmann's areas 5 and 7.

2. Lesions restricted to somatic area II seemed to be without effect on these tests, and the integrity of somatic area II could not compensate for a loss of somatic area I.

These results are discussed in relation to the adequacy of lesions and tests.

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Histopathology of the Mammillary Bodies in Alcoholic Psychosis

Silver carbonate techniques were used to examine degenerative changes in the brains of 4 alcoholic patients, 2 with Korsakoff's psychosis. The different types of histopathologic findings and their specificity are discussed.

Examination with silver carbonate suggests that the mammillary bodies are the site of peculiar forms of degeneration not encountered in other areas of the brain or in other pathologic conditions.

These changes can be summarized as (1) peculiar skein formations with the degenerated cell body in the centre and concentrically arranged fragmented processes, (2) fine fibrillary degeneration of the neurons, and (3) enlarged, rounded degenerated ganglion cells.

(Author's Abstr.)

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Influence of Mesencephalic and Diencephalic Stimulation on Limbic System Seizures

The effects of brain stem stimulation on electrically induced limbic system seizures were studied in 44 cats.

Brain stem stimulation was correlated with behavioural and electroencephalographic changes, and its influence on seizure production, propagation, duration, and variability was evaluated.

Seizures which were repeatedly and regularly produced had a tendency to maintain fixed characteristics. Furthermore, brain stem stimulation did not appear to alter the character of the discharge—except for its duration and variability.

Mesencephalic and hypothalamic stimulation seemed to reduce seizure duration and variability; the thalamus was inclined in the opposite direction. It must be emphasized that these structures displayed an almost equal ability to exert opposite effects from those assigned to them.

The effects of brain stem stimulation on seizures were interpreted as being both short and long lasting: short effects caused by direct neuronal stimulation, and long effects caused by induced humoral changes.

Seizure duration and variability appeared to be independent of the behavioural and electroencephalographic changes commonly described as activation.

Duration and variability changes from thalamic stimulation appeared to be independent of the thalamic recruiting responses.

Sleep spindles appeared more frequently during discharges from the cingulate gyrus than from other limbic structures and were not associated with increased seizure duration or propagation.

(Authors' Abstr.)

Studies on Abnormal Movement: Cerebellar Ataxia

1. Only 2 forms of ataxia, spinal and cerebellar, can be distinguished, but it is necessary to differentiate between these two entities and, further, between them and disequilibrium. Disequilibrium and cerebellar ataxia often occur together.

Disequilibrium affects the bodily musculature as a whole and is usually accompanied by deviation of the head and nystagmus. Disturbance at rest is evidenced by the assumption of tense postures and a strong disinclination to move. The head is involved in the kinetic and static disturbances which result. Wide, deviated, and lunging forms of locomotion with rolling, swaying, and twisting all may be seen in disequilibrium.

Cerebellar ataxia is characterized by forceful, springy, alternating activity which, if of cortical origin, interferes with the active attempt to arrange the limbs and body more particularly than with the effort to hold truncal postures, although so-called postural and intention, or, as we prefer to call them, ataxis, tremors are true manifestations of ataxia as are a great variety of special abnormal tests such as dysdiadochokinesis, abasia, and so on. It can be produced only by damage of the cerebellum itself or of its principal efferent pathway, the brachium conjunctivum, before division of the latter after its mesencephalic decussation.

Disequilibrium is evokable not only by injury to the vestibular system proper but also by interference with the flocculonodular lobe and its associated deep nuclei and connections. Spinal ataxia is due to destruction of afferent mechanisms at spinal levels. It is a loose, non-repetitive, throwing type of disarrangement, which occurs primarily in the lower extremities. (Authors' Abstr.)

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The Diagnostic Problem: Epilepsy of Late Onset

1. A follow-up study is presented of 141 patients with epilepsy of onset after the age of 20 who were seen at the National Hospital for Nervous Diseases, London.

2. Only 16 have been shown to have cerebral tumors. Of the others, 56 are believed not to have tumors on the basis of anatomic investigations by air encephalography or arteriography or both, plus a follow-up period of not less than three years; 20 other patients are believed not to have tumor on the basis of a fifteen-year follow-up alone. Additional tumors may yet be found among the remaining 49, but reasons are presented why these should not be numerous nor invalidate statistical comparison of the 2 groups.

3. The following circumstances significantly increase the likelihood of tumor to 28 to 50 per cent. and warrant contrast roentgenogram study:

Abnormal physical neurologic signs, the best single criterion;
Focal motor seizures or seizures with focal sensory aura;
Focal abnormality in the electroencephalogram (rare in this study unless the seizures were also focal);

Initial onset of fits in a patient over 50 years old.

4. Anatomic investigation is ordinarily not warranted in epileptic patients of adult onset who do not satisfy at least one of the above criteria—provided a satisfactory future follow-up can be made.

5. Even epilepsy of more than ten years' duration may be based on cerebral tumor—without the tumor killing the patient or being obvious. Failure to find abnormal physical neurologic signs in a patient who has been having fits for as long as three years, however, is a strong argument against the presence of a tumor, unless the seizures or the electroencephalograms are focal or the patient is more than 50 years old.

6. Even a normal air encephalogram at initial investigation does not rule out the possibility of tumor, and this diagnosis was made subsequently in 2 patients who were reinvestigated after a year's time because signs and symptoms had progressed. The need for follow-up is thus not obviated by any initial study.

(Authors' Abstr.)

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Physiologic Consequences of Total Hemispherectomy in the Monkey

An entire cerebral hemisphere, including the thalamus, can be successfully extirpated from the brain of rhesus monkeys at a single operation without interference with consciousness and with only moderate reduction in motor and sensory function. The operative procedure and resulting physiologic implications are discussed.

(Authors' Abstr.)

Ethoxzolamide—A New Anticonvulsant

The anticonvulsant effect of a new carbonic anhydrase inhibitor, ethoxzolamide, was studied. In a group of 25 epileptic patients who had been under poor control in spite of trials on virtually all commercially available anticonvulsant agents, 19 were found suitable for prolonged study over a seventeen-month period of time.

Most patients with grand mal and petit mal seizures were brought under excellent control; the improvement of patients with psychomotor seizures was significant but less striking. Side-effects necessitated termination of treatment in 2 of 25 patients, but toxic effects in the remainder were minimal. Because of its high potency as a carbonic anhydrase inhibitor, ethoxzolamide appears to be a significant addition to the growing number of anticonvulsant agents.

(Authors' Abstr.)

Treatment of Narcolepsy with Ritalin

Narcolepsy in 60 patients was treated by methyl phenidate hydrochloride (Ritalin hydrochloride) for eight to twenty-seven months. Good to excellent relief of abnormal sleepiness was reported by 49. Concurrent improvement of the cataplectic attacks occurred in 15 of 27 patients who had this symptom. Of the patients in the authors' original report whose condition could be followed, 68 per cent. reported good to excellent results after prolonged use; the comparable figure in their earlier study was 84 per cent. Side-effects were common but were usually minor.

The authors still believe that Ritalin is the drug of choice in the treatment of narcolepsy. In their experience, an initially satisfactory result can be maintained after prolonged use of this agent.

(Authors' Abstr.)

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Drugs for Treatment of Depression

The use of Marsilid produces remarkable improvement in the depressive syndromes because of the drug's antidepressive and psychic energizing properties. Marsilid can energize

the patient and yet does not overstimulate him. The authors have observed improvement in depressed patients regardless of diagnostic category, but, they repeat, Marsilid has little effect on many of the psychotic symptoms that may be present and sometimes increases psychopathologic processes. The tranquilizers are still superior in treating overt psychotic behaviour; however, in patients on long-term therapy—twelve to twenty months—discontinuance of Marsilid caused a return of delusions and hallucinations. Apparently, some psychopathology may be alleviated by long-term therapy with a psychic energizer.

The authors believe their studies during a twenty-month period leave no doubt that Marsilid is a unique antidepressive or psychic energizer. The Pavlovian theory that depression is a form of inhibition due to excessive stimulation must be seriously questioned.

Considerable doubt remains as to whether Marsilid's inhibition of amine oxidase in the brain is the drug's only essential function. At this time, they are evaluating the energizing action of other amine oxidase inhibitors and psychopharmaceutical agents.

The possible hepatotoxic effects of Marsilid are at present restricting the rational use of this drug by those clinicians who do not look at facts. Marsilid is unique, and no replacement is available. Since Marsilid is used as therapy and as an investigational tool, its loss cannot be evaluated.

Cause of possible toxic action must be determined, whether due to previous liver disease and existing pathology, augmentation of pathologic processes associated with infectious hepatitis, competition with vitamin B₆, chelation and removal of copper from essential oxidative enzyme systems, complex formation with adrenochrome, or unsuspected factors.

The history of science is not simply the history of discoveries and new ideas that tend to approach closer to reality. It is also the history of the defense of these findings against errors due to propaganda, politics, and bureaucracy.

(Authors' Abstr.)

Modification of Metrazol-Induced Convulsions by Ablations of the Brain

1. After ablation of the telencephalon, the salamander has co-ordinated walking, righting, and swimming; corneal and abdominal reflexes; and positive responses to tactile and visual stimulation. Intra-abdominal injection of Metrazol induces seizures with tonic and clonic components, hypersensitivity, gasping, and writhing.

2. After ablation of the prosencephalon, Metrazol induces a seizure with an extreme, tonic phase but hypersensitivity and the clonic phase are lost.

3. When both the prosencephalon and mesencephalon are removed, the salamander still walks, rights itself, and swims but Metrazol fails to evoke seizures with tonic and clonic components.

4. The salamander still has an abdominal reflex and withdraws the limbs when touched after the entire brain is excised, but injection of Metrazol is followed mainly by writhing and erratic placement of limbs.

5. The relationship of these observations to some aspects of phylogenetic development and to walking, localization of some seizure phenomena, and the mode of action of Metrazol is discussed.

(Authors' Abstr.)

Hallucinatory Effect in Man of Acetylcholine Inhibitors

1. In cats, 5,000 r. of 250-kv. X-ray were given to the exposed lumbar spinal cords. Some of the animals were observed for clinical effect, and some were studied for electrophysiologic changes in spinal cord reflexes.

2. Some early weakness was observed but completely disappeared in twenty-four hours. Complete paraplegia developed on the sixth or seventh day.

3. Anterior root responses to posterior root stimulation before and immediately after irradiation were investigated. By the fifth hour after irradiation, response time became significantly delayed. This delay meant conduction rates were slower. The total length of time of the response was not significantly changed until nine to ten hours after irradiation. The polysynaptic response gradually diminished in amplitude, and eleven hours after irradiation, was almost absent. At this time, the monosynaptic spike showed marked reduction in amplitude but was never more than a single spike. This later suggested cellular or synaptic alterations.

4. The effect of pentobarbital on the cat electroencephalogram was investigated; 6 fairly distinct electroencephalographic patterns were found associated with increasing depth of anesthesia. As the cat goes into lower levels of anesthesia, the anterior root response with posterior root stimulation is significantly altered; pentobarbital should not be used when this response is being studied.

(Authors' Abstr.)

Disseminated Sclerosis

1. An attempt was made to contact and study all persons in whom the onset of disseminated sclerosis occurred while they were living within a given district.

2. No evidence was found within the district studied that areas of high prevalence occurred, except for the Kingston area.

3. This high prevalence in Kingston was further examined and thought to be due to errors in sampling.

4. The suggestion is made that similar errors may have occurred in other cases where variations in incidence or prevalence have been reported.

(Authors' Abstr.)

Re-evaluation of Lumbar Puncture

Lumbar puncture was performed in 70 patients with papilledema and 59 patients with increased cerebrospinal fluid pressure without papilledema. The incidence of *possible* complications—any unfavourable changes within forty-eight hours—was significantly higher in the group without papilledema. Complications that did occur were probably not caused by lumbar puncture. From this study and a review of similar studies from the literature, one can say that the actual complications of careful diagnostic lumbar puncture in the presence of papilledema are much less than 1·2 per cent.

Use of careful lumbar puncture in the diagnosis and management of patients with papilledema is of definite value and may prevent unnecessary ventriculography or surgery. Therefore, the authors conclude that papilledema and increased intracranial pressure are not absolute contra-indications to careful, diagnostic lumbar puncture. Lumbar puncture should be performed to aid in diagnosis or management of the patients with papilledema or increased intracranial pressure.

(Authors' Abstr.)

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 Eosinophilia of the Cerebrospinal Fluid of Noninfectious Origin. *Kessler, L. A., and Cheek, W. R.* 371

Neurologic Aspects of Porphyria

A report is presented of 2 patients with acute intermittent porphyria and involvement of the nervous system. The clinical picture was that of progressive, peripheral polyneuropathy, predominantly motor in its manifestations. In 1 patient, diffuse cerebral involvement occurred. Both patients died of respiratory paralysis. The pathologic changes were those of a non-specific parenchymatous neuropathy with associated spinal root involvement of a lesser degree. In the central nervous system, axonal chromatolysis of cells occurred in the anterior horn and vagal nuclei. Nonspecific changes took place which were consistent with respiratory death.

The pathophysiology is considered to be an abnormality in the metabolism of porphyrin and purine compounds. Resulting disturbance of intracellular enzymes is reflected in widespread functional nervous system changes.

(Authors' Abstr.)

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Study of Lipids in Cerebrospinal Fluid. VI. The Normal Lipid Profile

1. An analytic scheme is presented for the duplicate determination of cephalins, cephalins plus lecithin, sphingomyelin, total phospholipid, total sphingolipid, total cholesterol, free cholesterol, and total lipid in 10 c.c. of cerebrospinal fluid. From these determinations, the

lecithin, cerebroside, cholesterol ester, total phospholipid, and neutral fat concentration can be calculated. The tests of the method were briefly reviewed.

2. The average, the s.e.m., and the range were given for these lipids in 27 healthy men and women 20 to 34 years old. Sphingomyelin, total phospholipid, and total lipid were significantly higher in men than in women; free cholesterol was lower in men. The rest of the lipid fractions were similar in both groups.

3. These data confirm certain reports in the literature that lumbar cerebrospinal fluid from normal individuals contains such lipids as cholesterol and phospholipids. In addition, the data indicate for the first time that cephalins, lecithin, sphingomyelin, cerebroside, and neutral fat are also present in normal spinal fluid.

4. The lipids in the normal spinal fluid were compared to those in normal fasting serum. On the average, the lipids in the serum were 514 times more concentrated. Furthermore, a similarity was apparent in the per cent. distribution of the lipids in normal spinal fluid and serum. However, if the data were expressed in terms of micrograms of lipids per milligram of protein, the differences between the various lipids in serum and spinal fluid were approximately 2.

(Author's Abstr.)

Function of Astroglia in the Water-Ion Metabolism of the Central Nervous System

In the present work, no change in the water content of the rat brain was found in a series of experiments leading to the increase of the general extracellular space such as bilateral nephrectomy followed by injection of large doses of isotonic solution or a similar treatment after craniectomy. Hydric intoxication with water and Pitressin in normal and craniectomized rats also did not change the water content of the brain. In all these cases, electron microscope study showed no alteration in the structure of the central nervous system.

Electron microscope study of the zone of "traumatic edema" in stab wounds of the brain of rats and rabbits showed that this type of lesion is not a true edema and that swelling is mainly located in the astrocytes.

Considerable increase in water content of brain slices was obtained after incubation in an isotonic solution for thirty to sixty minutes. The electron microscope study showed that the swelling is not due to the increase or to the formation of an extracellular space but to a considerable swelling of astroglia. Incubation in a hypotonic solution produced more marked swelling, and even a hypertonic solution might cause mild swelling of astrocytes. In all cases, neurons were not swollen and even showed compression of the perikaryon and dendrites by the swollen astrocytes.

On the basis of these morphologic and experimental evidences, it is concluded that there is no extracellular space or intercellular ground substance in the central nervous system. The conclusion is also reached that astroglia functions as a water-ion compartment in the central nervous system, which is involved in the selective transports of fluids and metabolites between the vascular system and the neurons.

(Authors' Abstr.)

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Physical Activity, Emotions, and Human Obesity

Caloric expenditure due to physical activity is a potentially important and largely neglected factor in human obesity. The present study indicates that decreased physical activity may play a role in the production and maintenance of the obesity of at least some persons.

Obese women appear to be far less active than non-obese women, and this difference in activity is paralleled by differences in attitudes toward activity. An investigation of the reasons for this decreased activity indicates that physical activity in man is determined by a variety of influences: biological, social, and emotional.

One of the most important and most common of these influences is the series of events associated with a depressive reaction pattern. Depression, thus, may not be a purely incidental occurrence in obese persons. It may be one of the main reasons why they are obese.

(Author's Abstr.)

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The Etiologic Significance of Emotional Factors in Onset and Exacerbations of Multiple Sclerosis: A Preliminary Report

On comparison of a series of MS patients with a control series certain features have been observed which seem to be typical of MS patients.

More often than can be due to chance, an unhappy childhood, rejection by both parents and especially by the mother, disturbed mother-child relationships, and erection of psychological defences against the feeling of being rejected have been outstanding features in the history of the MS patients studied.

Acute or chronic emotional disturbances frequently precede and apparently precipitate the onset of the disease, its relapses and exacerbations. Regardless of the specific nature of the disturbing events that precede the disease, they have in common the fact that they constitute a loss or a threat of losing a key figure in the patient's environment. MS is a disease that occurs frequently in chronically anxious individuals.

Deviation of sex behaviour and genital dysfunctions in the early stages of the disease seem to be related to the process of regression rather than to be due to organic lesions in the spinal cord.

The following preliminary observations have been made and conclusions have been drawn during the present study.

1. No uniformity of personality type prior to the onset of the disease could be detected. A broad range of personality structure was observed. Langworthy's view (1948, 1950) that patients suffering from MS are hysterical in make-up could not be confirmed.
2. Emotional and psychosexual immaturity due to early frustrations and deprivations leading to an infantilization of character formation which thus becomes vulnerable to psychosomatic disintegration in individuals with a "delicately poised security system" may be suggested as a specific dynamic constellation related to the onset, exacerbations, and relapses of MS.
3. A common feature in almost all the MS patients studied is the presence of morbid anxiety often antedating the onset of the disease by a considerable length of time and frequently reaching its peak prior to some attacks.
4. Emotional disturbances alone or in combination with such factors as physical stress and over-exertion, accidents, injuries, and other miscellaneous causes were most commonly thought of by the patients in the series as "causing" their disease.
5. MS is multicausal in origin. No claim for its psychogenesis has been made. But it has been demonstrated that more often than is generally known emotional factors play a part and may precipitate not only exacerbations and relapses of an established MS but even its onset.

(Authors' Abstr.)

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Metabolic Characteristics of Alcoholics. I. Response of Glucose Stress

1. Total leucocytes, urinary sodium, and an unidentified diazonium-coupling compound were found to occur at significantly higher concentrations in a group of 22 male alcoholics than in a group of 22 nonalcoholic controls.
2. No significant differences between the two groups in response to glucose stress were observed; both exhibited similar decreases in numbers of leucocytes, lymphocytes and eosinophils.
3. The relationship of these findings to those reported earlier for psychotic individuals are discussed.

(Authors' Abstr.)

Metabolic Characteristics of Alcoholics. II. Serum Copper Concentrations in Alcoholics

Serum copper concentrations determined in patients admitted to a state mental hospital for the treatment of alcoholism averaged 174y (range 105-273), per 100 ml. in a group of 30 who were treated with chlorpromazine, and 176y (range 115-332) per 100 ml. in a group of 19 who received no drug therapy. In 20 normal controls the average was 123y (range 102-148) per 100 ml. The difference between the alcoholics and the controls was statistically significant ($t=5.7$, $p<.001$).

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ANGUS MacNIVEN
President 1960-61